The Basics of Intra-Operative Neurophysiological Monitoring for the Clinician

A Practical Guide

Edited by
Chulananda Goonasekera
and Emma-Jane Smith

The Basics of Intra-Operative Neurophysiological Monitoring for the Clinician

The Basics of Intra-Operative Neurophysiological Monitoring for the Clinician:

A Practical Guide

Edited by
Chulananda Goonasekera
and Emma-Jane Smith

Cambridge
Scholars
Publishing

The Basics of Intra-Operative Neurophysiological Monitoring for the Clinician: A Practical Guide

Edited by Chulananda Goonasekera and Emma-Jane Smith

This book first published 2021

Cambridge Scholars Publishing

Lady Stephenson Library, Newcastle upon Tyne, NE6 2PA, UK

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

ISBN (10): 1-5275-6618-8
ISBN (13): 978-1-5275-6618-7

TABLE OF CONTENTS

PREFACE

Modern intra-operative neurophysiological monitoring, or IONM, represents an enormous technological advance in modern neurosurgery. Its modalities are diverse and continually evolving, and there exists wide variability in its practice. Relatively few books have been written on the subject, and it can seem daunting and impenetrable to the uninitiated.

Recognising these hurdles, we set out to distil the expertise of our regional neurosciences centre into a collaborative multidisciplinary text. We hope that this practical guide will: serve as a foundation for the clinician new to IONM; promote mutual understanding and effective team working between the different disciplines involved in its application; and ultimately, enhance patient care.

CHAPTER 1

AN OVERVIEW

CHULANANDA GOONASEKERA
EMMA-JANE SMITH

What is intra-operative neurophysiological monitoring (IONM)?

Unlike most human organs, neural structures such as the brain and spinal cord do not have the capacity to regenerate after an insult. Such damage – intrinsic or extrinsic – is therefore frequently associated with subsequent permanent disability. The major aetiologies of neurosurgical morbidity involve tumour invasion and neural tissue compression, which often require urgent intervention.

Neurosurgery is therefore focussed on preventing any further, or secondary, neural injury from a primary insult, in order to secure the best possible long-term outcomes for patients. Resection of brain tumours and correction of spinal lesions constitutes a large proportion of this work. Surgical intervention must be meticulous in order to minimise damage to normal structures, and yet the differentiation of the latter from abnormal tissue is highly challenging. To better facilitate this crucial process, various "static" techniques exist, mainly based on superimposed anatomical imaging or tissue staining. Intra-operative neurophysiological (or simply neuro-) monitoring (IONM) techniques offer a novel, "dynamic", method for functional assessment of neural structures in real time.

In the 1930s, direct cortical stimulation was used to locate the motor cortex in patients with epilepsy (Penfield and Boldrey 1937). Decades later, more sophisticated IONM techniques began to emerge (Nuwer 2008), but it was not until the 1990s that one particular modality – transcranial motor evoked potentials (TcMEPs) – became an established method of monitoring corticospinal tract activity. Today, IONM has

become a dynamic aid in intra-operative decision-making and a primary tool for the prediction of neurological outcome (Kothbauer, Deletis, and Epstein 1997). It provides a real-time functional mapping technique to discriminate between normally functioning and dysfunctional structures in the anaesthetised patient. The method employs various electrodes to observe the spontaneous electrical activity of the brain and its reactions to stimuli. Multimodal IONM enables monitoring of a variety of neural structures including the cortex, brainstem, peripheral nerves, neuromuscular junction and spinal cord (Stecker 2012) (Kim et al. 2013). In practice, surgery involving "eloquent" cortex (areas in which damage is prone to cause major focal neurological deficits) may still require traditional Stagnara "wake-up" testing, in which anaesthesia is lightened intra-operatively and the patient asked to follow various commands in order to verify functional integrity (Vauzelle, Stagnara, and Jouvinroux 1973). However, the advent of IONM has successfully avoided this technique for many patients, especially children.

IONM in practice

Electrode placement

The placement of electrodes for IONM takes place after induction of general anaesthesia (NICE 2008). Corkscrew electrodes are attached to the surface of the scalp to monitor the spontaneous electrical activity of the brain. Needle electrodes may be implanted into the spine, limbs, tongue, eyes, ears, face or perineum to record evoked responses to various electrical stimuli (Legatt et al. 2016). The placement of these electrodes varies according to surgical field and neuromonitoring mode requirements. Mobile or dislodged electrodes may produce inaccurate results (Legatt et al. 2016) and so these must be secured with care.

Pre-surgical benefits

Suboptimal patient positioning for surgery is known to risk both neurological and vascular compromise, which can impact on IONM, as well as causing significant postoperative morbidity. This is of particular concern when substantial cervical spine flexion is necessary for surgical access, such as in the sitting or prone positions. Baseline motor and somatosensory evoked potentials are therefore commonly performed in the supine position following induction of anaesthesia, and then repeated once positioning is complete. This permits adjustment of position should a deterioration in

recorded potentials be detected prior to the start of surgery – in other words, a deficit arising as a result of imperfect positioning alone. However, vigilance must be maintained as changes may also occur intra-operatively if minor changes in position have taken place, such as from muscular contractions elicited by IONM. Changes in, or loss of, signals can also occur as a result of artefact from misplaced electrodes, or electrical interference from muscle activity or surgical equipment.

Modalities

There are numerous modalities of IONM. These are often used in combination during a single operation as each approach provides unique information (Kim et al. 2013); the use of a greater number of modalities also confers a higher margin of safety. A summary of the commonly used modalities is listed here.

Electro-encephalography (EEG) and Electrocorticography (ECoG)

An EEG machine records brain electrical activity using corkscrew needles placed in the postcentral parietal regions of the scalp (Kim et al. 2013). EEG recordings, best known for their ability to detect seizure activity, also provide information on the depth of anaesthesia. ECoG refers to similar readings but with electrodes placed directly on the exposed surface of the brain. This is also known as intracranial electro-encephalography or iEEG.

Electromyography (EMG)

EMG examines the activity of skeletal muscle fibres and may be either spontaneous or provoked ("triggered"). Needle electrodes are placed in certain muscle groups and electrical activity is recorded with or without concurrent electrical stimulation. The use of both spontaneous and triggered modes together leads to more effective anticipation and minimisation of damage to nerve roots (Lall et al. 2012).

Motor Evoked Potentials (MEPs)

This is a form of transcranial electrical stimulation, also known as transcranial motor evoked potentials (TcMEPs). Electrodes on the scalp stimulate the primary motor cortex to examine the integrity of the descending corticospinal tracts. MEP monitoring contributes to deficit

prevention during the resection of tumours of the cerebral cortex and spinal cord, and is highly specific and sensitive in predicting postoperative neurological deficit (Rho, Rhim, and Kang 2016). It is also used to detect spinal cord ischaemia during thoracic aortic reconstruction.

Muscle Motor Evoked Potentials (mMEPs)

These refer to the recording of muscle contractions generated from needle electrodes inserted directly into muscles. Both MEPs and mMEPs can only be assessed intermittently during surgery as they may cause significant patient movement. This necessarily interrupted assessment invites the risk of delay in identifying neurological damage.

Somatosensory Evoked Potentials (SSEPs)

SSEPs are recordings of ascending sensory signals to monitor the dorsal column–medial lemniscus pathway (Lall et al. 2012). Stimulating electrodes are frequently placed over the median and ulnar nerves in the upper limb, and the posterior tibial nerve in the lower limb (Lall et al. 2012). Signals are recorded via electrodes placed on the scalp. Unlike MEPs, SSEPs can be continuously monitored during surgery.

Visual Evoked Potentials (VEPs)

VEPs assess the visual pathway. A device that produces flashes of light is placed over each closed eyelid. The electrical potentials generated by these brief visual stimuli are recorded via scalp electrodes.

Brainstem Auditory Evoked Potentials (BAEPs)

These potentials are generated by auditory stimulation of the vestibulocochlear nerve. This reduces the risk of damage to this cranial nerve during surgery involving its course, such as resection of acoustic neuromata (Kim et al. 2013).

Anaesthetic implications of IONM

Although neuromonitoring confers attractive advantages, its accuracy is dependent on the fulfilment of multiple preconditions and major modifications to anaesthesia (Cabraja et al. 2009).

Physical conditions

Signal recordings are vulnerable to changes in physical parameters such as body temperature, blood pressure and haemoglobin concentration, which the anaesthetist must strive to keep at optimal levels. The maintenance of stable conditions is particularly challenging during procedures involving significant blood loss or tissue irrigation.

Anaesthetic agents

Many anaesthetic drugs impact on the use of IONM, with the effects being dependent on several variables including type of agent, dosage, and mode of neuromonitoring in question (Banoub, Tetzlaff, and Schubert 2003). Evoked responses which travel via polysynaptic pathways, such as VEPs, are significantly more susceptible to the vagaries of anaesthesia and surgical conditions when compared to pathways with fewer synapses (Soghomonyan et al. 2014).

Inhalational agents such as sevoflurane are commonly used for anaesthetic maintenance but are potent suppressants of evoked potentials, rendering many forms of IONM uninterpretable. Intravenous anaesthetic drugs confer much less interference, hence the popularity of total intravenous anaesthesia (TIVA) for maintenance of anaesthesia during IONM. TIVA is characterised by continuous intravenous infusions of anaesthetic drugs, typically the anaesthetic agent propofol in combination with the ultra-short-acting synthetic opiate remifentanil. Administration is titrated to the individual patient according to clinical parameters and supplementary depth of anaesthesia (DOA) monitoring.

Neuromuscular blocking agents (NMBAs) also interfere with IONM. This is most apparent in EMG and MEP monitoring, as signal transmission across the neuromuscular junction is partially or totally impeded. Consequently, the use of these drugs is either restricted to induction of anaesthesia in order to facilitate endotracheal intubation (with preference given to shorter-acting agents), or avoided entirely (Kim et al. 2013).

Depth of anaesthesia monitoring

Bispectral Index (BIS), E-Entropy and Narcotrend Compact M are all patented examples of DOA monitoring, with BIS being the most commonly encountered at the time of writing. All are primarily based on processed EEG signals and allow the dose of anaesthetic agent to be

tailored to the individual patient. This aims to reduce the risk of both underdosage (with an attendant risk of awareness under general anaesthesia (AAGA)), and overdosage (with its associated cardiovascular side effects and prolonged recovery from anaesthesia). The use of DOA monitoring is considered the standard of care during TIVA, and therefore most cases involving the use of IONM; however, it is not without limitations. BIS, for example, is based on information from just four electrodes, and is susceptible to inference from muscle activity and altered cerebral perfusion. Clinicians must be mindful of these shortcomings and assimilate the range of available clinical information to gain an accurate impression of anaesthetic depth.

Electrode placement

Electrodes may be sited in areas of particular concern to the anaesthetist, including the vocal cords, soft palate, tongue and eye muscles. Such placement is typically necessary when cranial nerve monitoring is being undertaken, for example in brainstem or posterior fossa surgery. In addition to electrode location, the anaesthetist must also anticipate the muscular contractions that follow intermittent intra-operative stimulation: a soft “bite block” between the molar teeth helps to avoid intra-oral injury from jaw clenching, for example.

Adverse events

IONM and the modifications to anaesthetic technique that it necessitates invite added risks, including AAGA, seizures, cardiac dysrhythmias, dental and oral damage and calf muscle injury; very rarely, severe injury such as bone fracture may occur. These risks are mitigated by DOA monitoring, bite blocks, careful positioning and most importantly, intra-operative vigilance.

The neuromonitoring team

The combined knowledge and experience of the surgeon, anaesthetist, neurophysiologist and wider theatre staff is crucial to obtain meaningful and reliable IONM results (Kim et al. 2013). Communication between these specialist roles is imperative for the successful application of neuromonitoring, as is understanding of the surgical procedure, neurophysiology and the effects of general anaesthesia (Stecker 2012). The detection of IONM signal changes must be swiftly communicated to the

rest of the team to enable a coordinated response to prevent injury to the patient. IONM should be discussed at the presurgical team briefing and incorporated into local versions of the World Health Organisation (WHO) Surgical Safety Checklist.

Ethics and research

Although the theoretical benefits of IONM are clear and its use continues to increase (Soghomonyan et al. 2014), information on its efficacy, complications and patient impact remains sparse. As a technique, it remains a prototype and continues to evolve (Rho, Rhim, and Kang 2016) (Sala 2010). There currently exists no uniform standard of care or evidence-based guideline for neuromonitoring across all centres, as the methods employed are diverse and developed based on the experience and understanding of local teams. Nonetheless, IONM is considered by many to be the gold standard for the intra-operative prevention of inadvertent neuronal injury (Coppola et al. 2016).

Current research investigating IONM is directed mainly towards exploring the physiology and efficacy of the technique (Cabraja et al. 2009), but studies are also needed to elucidate its influence on outcomes, associated postoperative morbidity and patient experience. The recurrence of tumours after neurosurgery guided by IONM, and the potential humoral effects of electrical stimulation on tumour behaviour, are other areas which remain as yet unexplored.

References

Banoub, M., J. E. Tetzlaff, and A. Schubert. 2003. "Pharmacologic and physiologic influences affecting sensory evoked potentials: implications for perioperative monitoring." *Anesthesiology* 99 (3):716-37.

Cabraja, M., F. Stockhammer, S. Mularski, O. Suess, T. Kombos, and P. Vajkoczy. 2009. "Neurophysiological intraoperative monitoring in neurosurgery: aid or handicap? An international survey." *Neurosurgical Focus* 27 (4):E2.

Coppola, A., V. Tramontano, F. Basaldella, C. Arcaro, G. Squintani, and F. Sala. 2016. "Intra-operative neurophysiological mapping and monitoring during brain tumour surgery in children: an update." *Childs Nervous System* 32 (10):1849-59.

Kim, S. M., S. H. Kim, D. W. Seo, and K. W. Lee. 2013. "Intraoperative neurophysiologic monitoring: basic principles and recent update." *Journal of Korean Medical Science* 28 (9):1261-9.

Kothbauer, K., V. Deletis, and F. J. Epstein. 1997. "Intraoperative spinal cord monitoring for intramedullary surgery: an essential adjunct." *Pediatric Neurosurgery* 26 (5):247-54.

Lall, R. R., R. R. Lall, J. S. Hauptman, C. Munoz, G. R. Cybulski, T. Koski, A. Ganju, R. G. Fessler, and Z. A. Smith. 2012. "Intraoperative neurophysiological monitoring in spine surgery: indications, efficacy, and role of the preoperative checklist." *Neurosurgical Focus* 33 (5):E10.

Legatt, A. D., R. G. Emerson, C. M. Epstein, D. B. MacDonald, V. Deletis, R. J. Bravo, and J. R. Lopez. 2016. "ACNS Guideline: Transcranial Electrical Stimulation Motor Evoked Potential Monitoring." *Journal of Clinical Neurophysiology* 33 (1):42-50.

NICE. 2008. Intraoperative nerve monitoring during thyroid yroid surgery. edited by National Institute for Health and Care Excellence. Manchester: National Institute for Health and Care Excellence.

Nuwer, M. R. 2008. "Intraoperative Monitoring of Neural Function." In *Handbook of Clinical Neurophysiology*, edited by Marc Newer, 1-955. New York: Elsevier Ltd.

Penfield, W., and E. Boldrey. 1937. "Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation." *Brain* 60 (4):389-443.

Rho, Y. J., S. C. Rhim, and J. K. Kang. 2016. "Is intraoperative neurophysiological monitoring valuable predicting postoperative neurological recovery?" *Spinal Cord* 54 (12):1121-1126.

Sala, F. 2010. "Intraoperative neurophysiology is here to stay." *Childs Nervous System* 26 (4):413-7.

Soghomonyan, S., K. R. Moran, G. S. Sandhu, and S. D. Bergese. 2014. "Anesthesia and evoked responses in neurosurgery." *Frontiers in Pharmacology* 5:74.

Stecker, M. M. 2012. "A review of intraoperative monitoring for spinal surgery." *Surgical neurology international* 3 (Suppl 3):S174-87.

Vauzelle, C., P. Stagnara, and P. Jouvinroux. 1973. "Functional monitoring of spinal cord activity during spinal surgery." *Clinical Orthopaedics & Related Research* 93:173-8.

CHAPTER 2

HISTORICAL ASPECTS

PRIYANKA IYER

Introduction

The need for a monitoring technique of the spinal cord arose alongside evolving surgical techniques, such as that of corrective surgery for severe scoliosis (Harrington 1962). Intra-operative neurophysiological monitoring (IONM) was born as a consequence, with the overarching aim of preventing neurological deficits following surgery. It is a mapping and monitoring technique which assesses the integrity of neuronal structures during brain and spinal surgery (Sala 2010), and has become a valuable method of intra-operative neurological assessment (Stecker 2012). The use of IONM nowadays frequently eliminates the need for conventional wake-up testing during neurosurgery, with the exception of procedures involving areas relating to more complex functions, such as speech.

This chapter highlights the major milestones and discoveries that have contributed to modern-day intra-operative monitoring of the motor and sensory tracts.

Origins

Hans Berger is credited with the invention of electro-encephalography (EEG) in the 1920s, with the alpha wave still occasionally bearing his name ("Berger wave") (Penfield and Boldrey 1937). Electrical activity in muscle was first recorded by Du Bois-Reymond (Penfield and Boldrey 1937).

In 1935, intra-operative internal EEG (electrocorticography or ECoG) was used for locating the motor cortex in patients with epilepsy (Penfield and Boldrey 1937). The investigators published a complete analysis of the

records of 163 patients whose cortices they had electrically explored under local anaesthesia. The challenges of the rudimentary mapping procedure were significant, with the authors noting that it was “impossible to confine functional representation within strict cyto-architectural boundaries” (Penfield and Boldrey 1937). The authors highlighted the crucial role of the anaesthetist, who was required to follow the movements and behaviour of the patient, as well as monitor blood pressure, heart rate and other parameters. Neurostimulation was carried out by either unipolar or bipolar platinum electrodes with a thyratron stimulator, employing a wave frequency of 55-65 Hz.

Shortly after the debut of the EEG, somatosensory evoked potentials (SSEPs) were developed in the 1940s (Liem 2016). Despite these two significant initial advances, IONM as a technique then stagnated for several decades (Nuwer 2008). The first transcranial motor evoked potentials (TcMEPs) were recorded in 1980 (Merton and Morton 1980), but this only became an established method of monitoring corticospinal tract activity in the 1990s. This delay was mainly due to the available anaesthetic agents of the day significantly interfering with the evoked potentials produced. TcMEPs have since been used to monitor the functional aspects of not only the corticospinal motor tracts, but also spinal nerve roots, peripheral nerves, and nerve plexuses (Devlin and Schwartz 2007).

In conjunction with scientific developments, industry played an important role through advances in commercial multi-channel IONM equipment (Kim et al. 2018). Prior to the availability of such equipment, neurophysiologists frequently devised or modified their own.

The uptake of IONM across the world owes as much to advances in technology as it does to scientific endeavour. Currently the technique is increasing in usage and is recognised as the gold standard for the location and preservation of brain function during surgery (Sala 2010) (Coppola et al. 2016).

Monitoring the sensory pathways

Spinal Cord Evoked Potentials (SCEPs): stimulation of the spinal cord

American surgeon and polio specialist Jacquelin Perry was the first to highlight the need for intra-operative spinal cord monitoring (Tamaki and

Kubota 2007). A team led by Tamaki later began to investigate the feasibility of recording SSEPs during orthopaedic surgery. The research group visited the laboratory of Sidney Goldring at Washington University, whose research at the time was focused on the effects of anaesthesia on SSEPs (Kelly, Goldring, and O'Leary 1965). Tamaki discovered that the instruments involved were large and costly, and required electrical engineers to correctly operate them. In search of mitigation for these impracticalities, in 1972 Tamaki pioneered technology to enable direct stimulation of the spinal cord via the epidural space, producing a spinal cord evoked potential (SCEP), also known as a "D" wave (Kurokawa 1975). Potentials produced via these means were large in amplitude and could be easily recorded with basic electrical hardware in the operating theatre. An example of a SCEP is illustrated by Figure 2-1. The disadvantage to the technique was the need for invasive introduction of the stimulating and recording electrodes into the epidural and intrathecal spaces respectively – procedures which carried significant risks. An example of a modern epidural electrode is illustrated in Figure 2-2.

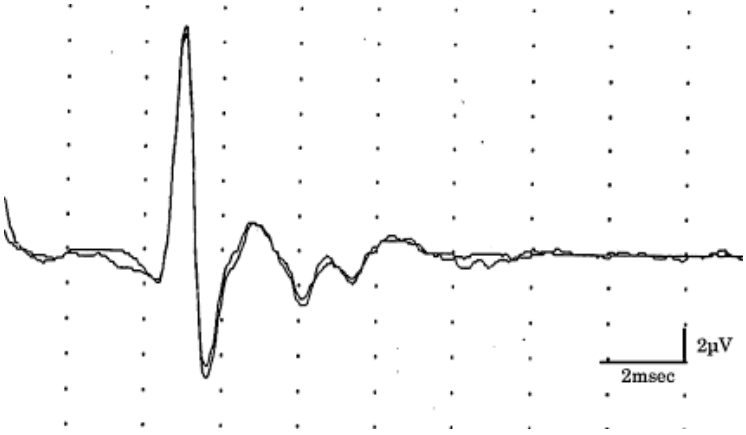

Fig. 2-1. A spinal cord evoked potential (SCEP) recorded at the level of T12 after stimulating the spinal cord at C7. The potential demonstrates an initial spike wave, followed by polyphasic waves. The summation of potentials from large diameter fibres in the posterolateral columns results in the initial high amplitude spike, with the subsequent smaller waves mainly reflecting dorsal column stimulation. Reproduced with permission (Tamaki and Kubota 2007).

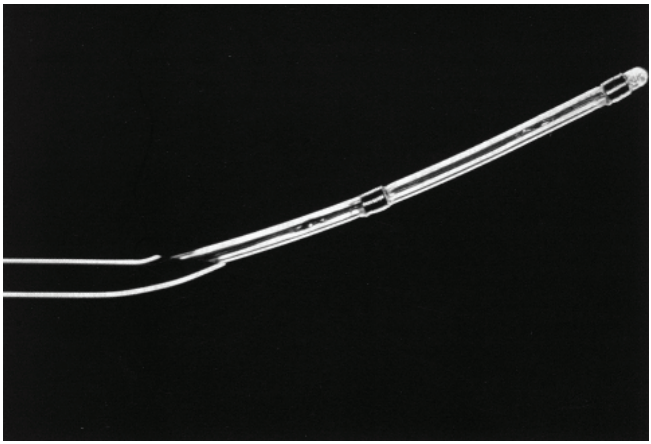

Fig. 2-2. A specially designed electrode comprising a flexible polyethylene tube with two coils of platinum wire, suitable for introduction into the epidural and intrathecal spaces. Reproduced with permission (Tamaki and Kubota 2007).

In essence, the SCEP represents a signal derived from both ascending and descending tracts passing close to a recording electrode. Unlike sensory potentials which are large in amplitude, motor potentials are more subtle, meaning that information from the descending tracts is more difficult to accurately record and interpret. False negative recordings – when neurological damage occurs insidiously and is not detected by signal changes – have been previously reported (Iwasaki et al. 2003). In a case series published by Koyanagi and colleagues, both false positive and false negative results were observed (Koyanagi et al. 1993). The authors' proposed reasons for these observations included inaccurate positioning of the stimulating electrode, differing thresholds in electrical stimulation of axons on the left and right sides of the spinal cord, and changes in distance between the electrode and spinal cord surface. It was therefore suggested that SCEP be used in combination with other types of evoked potentials to increase reliability.

Somatosensory Evoked Potential (SSEPs): stimulation of a peripheral nerve

SSEP recordings are the most widely used modality in the spectrum of IONM. This non-invasive technique was initially introduced by Nash and colleagues in 1972, who demonstrated its use in patients undergoing scoliosis correction (Croft, Brodkey, and Nulsen 1972). The method

involves recording potentials by stimulating peripheral afferent nerves, with ascending impulses travelling through the dorsal column and culminating in the sensory cortex. The median nerve at the wrist is most frequently used for upper limb monitoring, whilst the lower limb equivalent is the posterior tibial nerve. Recording electrodes for both extremities are placed on the scalp (Figure 2-3). The slower-conducting spinothalamic pathway fibres are not monitored by this technique.

Later in the same decade, Nash reported a series of orthopaedic and neurosurgical patients in whom somatosensory cortical evoked potentials were used to monitor spinal cord integrity before, during and after their procedures (Nash et al. 1977). They concluded that the technique was effective, had few inherent risks in its application, and had the potential to greatly improve the safety of spine and spinal cord surgery.

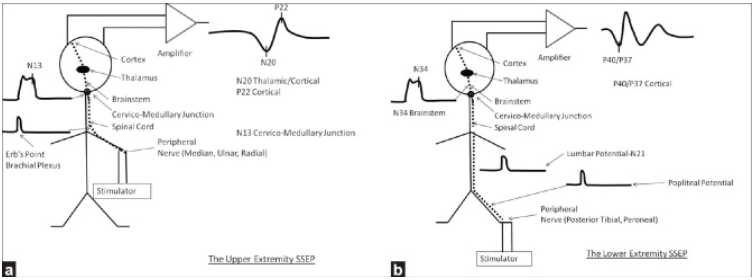

Fig. 2-3. Somatosensory evoked potential schematics from the upper and lower extremity. Reproduced with permission (Stecker 2012).

Interestingly, intra-operative SSEP monitoring during cervical spinal surgery can also provide important information on the functional integrity of brainstem structures, with the resultant ability to detect brainstem ischaemia. This was illustrated by a case report of a patient undergoing posterior cervical fusion with bilateral SSEP monitoring (Tran et al. 2012). During initial exposure of the C1 lamina, the SSEPs became asymmetrically reduced, and a postoperative MRI scan demonstrated bilateral posterior inferior cerebellar artery (PICA) territory infarcts. The asymmetry of SSEP change was consistent with medullary level impairment, permitting lateralisation of the vascular territory. Conversely, anterior spinal artery insults typically result in symmetrical deficits. Thus, interpretation of SSEPs demands a sound knowledge of medullary anatomy and vascular territories.

SSEPs are not without risk of false negative results, which have been seen in cases including infratentorial tumours presenting with brainstem compression, small lesions of the motor cortex, and small vessel damage during aneurysm surgery (Wiedemayer et al. 2004). The use of SSEPs as the sole modality of IONM is therefore not recommended as it relies heavily on the integrity of the dorsal columns alone.

Spinal somatosensory evoked potentials (spinal SSEPs) were introduced in the same decade as SSEPs (Shimoji, Higashi, and Kano 1971). They involve recording spinal electrograms from within the epidural space. As spinal SSEPs reflect the activity of the ascending dorsal column tracts, they can be extremely valuable during posterior myelotomy for the removal of intramedullary spinal cord tumours. This technique was taken up in particular by the Royal National Orthopaedic Hospital in Stanmore, UK, where results from 115 patients concluded that spinal SSEPs could effectively detect even minor spinal cord impairment, with reversible changes seen after surgical intervention (Jones et al. 1983). All signals were detected in response to posterior tibial nerve stimulation at the knee, with recording electrodes in the epidural space being placed cephalad to the area being fused. The epidural recording electrodes were noted to be simple to insert and unobtrusive to the operating surgeon.

The rationale for monitoring motor tracts

Before the advent of directly testing the motor tracts during surgery, SSEP monitoring was used as an indirect measure. This technique relied on the anatomical proximity of the sensory and motor tracts, the premise being that pathology affecting the motor pathways would also manifest as disturbance in the sensory pathway, and the latter could be detected as a deterioration in the SSEP signal (Macdonald et al. 2013). Although SSEP monitoring was found to reduce the risk of paraplegia in spinal surgery by half (Nuwer et al. 1995), there have been cases noted in the literature where, despite unchanged intra-operative SSEPs, patients went on to demonstrate postoperative neurological deficits (Lesser et al. 1986). Possible explanations for this include: false negative results due to lesions outside the tract being assessed, for example motor deficits or below the level being monitored; pre-existing pathology that might render native tracts inaccessible to monitoring; technical problems that result in suboptimal recordings; and slowly progressive structural change either not immediately detectable, or detectable but irreversible in nature. As anaesthetic agents alone can affect the latency of the evoked potentials

intra-operatively, the authors stressed the importance of pre-set criteria which define an abnormality in signal.

Motor tract monitoring

The historical milestones leading to modern-day IONM are summarised in Figure 2-4. The observation by Fritsch and Hitzig in 1870 that directly stimulating the frontal cortex of dogs can produce contralateral movement was one of the earliest recorded instances of motor evoked potential (MEP) monitoring (Fritsch and Hitzig 2009). The implementation of this technique in humans during brain surgery was pioneered by Horsley and Foerster (Macdonald et al. 2013).

Beginning in 1886, Victor Horsley performed operations on patients that involved electrical stimulation of the cortex (Tan and Black 2002). His first three craniotomy patients at Queen Square, London had intractable seizures secondary to lesions such as cortical scars, tumours or cysts within or near the motor cortex, and therefore were expected to respond favourably to localised excision. At the time, resection of such cortical "motor points" was hailed as a promising treatment for focal seizures.

Several years later, highly-trained neurologist and self-taught neurosurgeon Ofrid Foerster began his career by operating on peripheral nerves during the First World War. Many of his early patients were war veterans with intractable posttraumatic epilepsy (Uematsu, Lesser, and Gordon 1992). Alongside local anaesthesia to facilitate cortical mapping, Foerster used unipolar galvanic stimulation to induce clinical seizures, permitting localisation and then excision of the responsible focus. By 1931, having gathered information on more than 150 cases of cerebral cortical stimulation, Foerster's experience surpassed that of any other neurosurgeon at the time.

A more advanced method known as the Penfield technique was later established by Penfield and Jasper, who routinely used direct cortical stimulation using a probe with 50-60 Hz pulse trains during epilepsy surgery (Penfield and Boldrey 1937) (Jasper 1952) (Jasper 1949). This was used as a surrogate test for cortical function, but the technique was only possible with local (as opposed to general) anaesthesia, hindering its widespread use. Soon after this, other methods of intra-operatively assessing cortical function and epileptic foci were trialled, including electrocorticography, electromyography, and nerve conduction studies (Walker, Johnson, and Marshall 1949).

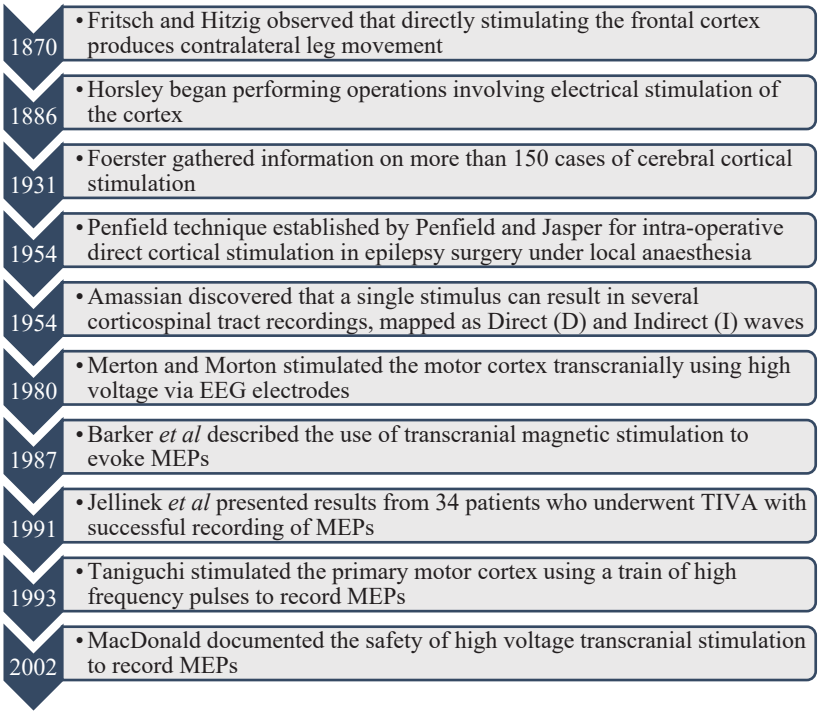

Fig. 2-4. Historical milestones in the development of motor tract monitoring.

The discovery by Amassian in 1954 that a single stimulus can result in several corticospinal tract signals which can be successfully mapped as a direct ("D") and indirect ("I") waves was the next milestone in the development of MEPs (Patton and Amassian 1954). D waves were represented by negative peaks – assumed to be represent direct activation of the corticospinal fibres – whilst I waves reflected high frequency repetitive discharges from the corticospinal tract (Figure 2-5).

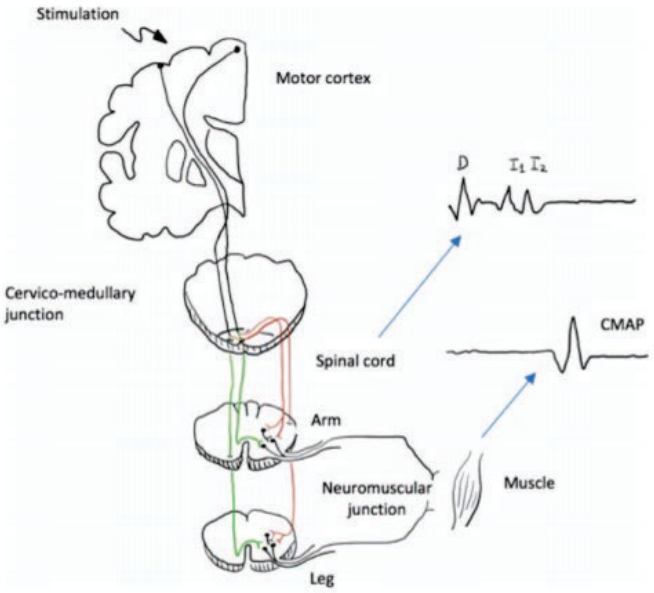

Fig. 2-5. Motor pathway monitored by motor evoked potentials, with the waveform recorded from both cord level (D and I waves) and muscle level (compound muscle action potentials). The red (right-hand) pathway reflects the majority of the motor fibres that reside in the lateral corticospinal tract after decussation at the brainstem level. The green (left-hand) pathway depicts the anterior corticospinal tract with fewer motor tracts. Reproduced with permission (Wing-hay and Chun-kwong 2019).

In 1980, Merton and Morton described stimulation of the motor cortex transcranially using a high voltage condenser (0.1 μF, charged to up to 2000 V) (Merton and Morton 1980). Electrodes placed on the scalp stimulated the primary motor cortex, thereby assessing the functional integrity of the descending corticospinal tracts (Figure 2-6). This technique successfully recorded evoked muscle action potentials. A major obstacle to its use in surgery was that the anaesthetic agents of the time – predominantly nitrous oxide and halogenated gases – inherently depressed motor neurone activity.

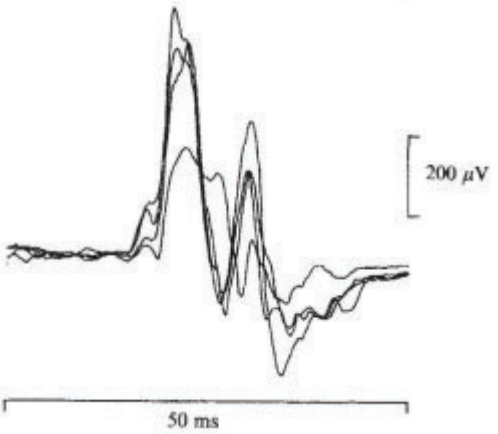

Fig. 2-6. Stimulation of the arm area of the motor cortex. These recordings represent the action potentials from the contracting muscles in the forearm. Reproduced with permission (Merton and Morton 1980).

In the same decade, a group of orthopaedic surgeons involved in corrective surgery for scoliosis recorded potentials from the scalp and spine after stimulation of the tibial nerve or the spinal cord in sixty patients. Similarly to cortical stimulation for MEPs, they found that recording meaningful muscle MEPs was difficult under general anaesthesia (Machida et al. 1985).

Boyd *et al* reported a case series of patients in whom high voltage stimulation (maximum output of 700 V, with a peak current of approximately 500 mA) was applied to the scalp over the motor cortex, with evoked motor potentials then being recorded by electrodes in the epidural space (Boyd et al. 1986). The authors described the technique as a useful adjunct to conventional sensory monitoring pathways, although placement of epidural electrodes was invasive with inherent risk, and the monitoring excluded lower motor neurones.

Similarly, Barker and colleagues described the use of transcranial magnetic stimulation to evoke MEPs, but again this could not be employed under general anaesthesia (Barker, Jalinous, and Freeston 1985). Paired cortical stimuli were introduced by others (Inghilleri et al. 1990) (Taylor et al. 1993) to overcome this problem, employing the principle of effective accumulation of excitatory post-synaptic potentials at the anterior horn motor neurones.

The introduction of total intravenous anaesthesia (TIVA) with agents such as fentanyl and propofol was a seminal event which finally rendered motor tract monitoring in the operating theatre feasible. Jellinek and colleagues presented results from 34 spinal surgery patients who underwent TIVA with propofol (Jellinek, Jewkes, and Symon 1991). Intra-operative monitoring of motor function with MEPs was successful in 88.5% of controls with normal pre-operative motor conduction; propofol was noted to cause a reduction in response amplitude of just 7% from baseline. Successful intra-operative monitoring was established in 87% of patients in the group with pre-existing abnormal neurology. Significant changes in both amplitude (greater than 50%) and/or onset latency (greater than 3 ms) were found within minutes of surgical manoeuvres, with three of the patients subsequently improving and a deterioration in motor function noted in two.

As already mentioned, a major hurdle in successfully measuring MEPs was to develop a technique that remained effective after the patient was anaesthetised. Taniguchi and colleagues first demonstrated a modification of the direct cortical stimulation technique that allowed MEPs to be recorded under general anaesthesia (Taniguchi, Cedzich, and Schramm 1993). Instead of the traditional method of applying a train of lower frequency impulses of the order of 50-60 Hz, the investigators stimulated the exposed primary motor cortex with a brief trains of high frequency pulses (300-500 Hz), with compound muscle action potentials (CMAPs) being recorded from the forearm and hand muscles. Their hypothesis was that this stimulation resulted in repetitive activation of the descending motor tract; it was found that surgical manipulation then demonstrably affected the motor pathways and the resultant MEPs.

Jones and colleagues were one of three groups that successfully demonstrated MEPs under anaesthesia in response to transcranial electrical stimulation (Jones et al. 1996). They monitored 22 patients anaesthetised with propofol, with or without nitrous oxide. Responses were consistently measurable in every patient but one, and the investigators concluded that the technique was especially useful in patients with myelopathy in the thoracic region. Pechstein *et al* found that instead of single pulse transcranial stimulation, high frequency repetitive electrical stimulation could evoke myogenic MEPs that recordable in forearm flexors, thenar and hypothenar muscles (Pechstein et al. 1996).

Development of electrical hardware in the form of a high-voltage transcranial stimulator manufactured by Digitimer Ltd enabled the

widespread use of motor tract monitoring. Its clinical safety was documented by MacDonald, who compared the safety of transcranial MEP monitoring with that of other brain stimulation methods in over 15,000 cases and found few adverse neuropsychological events (MacDonald 2002). This review concluded that the benefits of this modality outweighed the risks when applied to carefully selected patients under expert supervision.

Currently, electrical or magnetic stimulation of the motor cortex is used to obtain recordings of action potentials: either in the distal spinal cord or peripheral nerves as neurogenic potentials, or in muscle as myogenic potentials. Stimulating the brain electrically, either through electrodes on the scalp or directly on the cerebral surface, produces a current within the motor cortex which progresses primarily through the lateral corticospinal tract. Alternative methods include applying a pulsed magnetic field over the scalp.

Other IONM adjuncts

Brainstem Auditory Evoked Potentials (BAEPs)

Stimulation of the vestibulocochlear nerve by auditory stimuli to generate brainstem auditory evoked potentials (BAEPs) was introduced in 1982. BAEPs and EMG were later integrated into IONM with the aim of minimising the risk of damage to the eighth cranial nerve, which is particularly at risk during the surgical management of infratentorial lesions. Moller and colleagues reported data from 143 cases of microvascular decompression of the facial nerve for the surgical management of hemifacial spasm (Moller and Moller 1985). Due to the anatomical proximity of the vestibulocochlear nerve, a proportion of patients also underwent direct monitoring of auditory compound action potentials. Of all the cases, four patients reported profound hearing loss postoperatively, three of whom had not received intra-operative auditory monitoring. The fourth patient lost his hearing despite having been monitored. The reliability of BAEPs have therefore been questioned, with technical difficulties arising from detection of the potentials themselves.

Visual Evoked Potentials (VEPs)

Adrian and Mathews were one of the first to successfully record visual evoked potentials (VEPs) (Adrian 1936) (Adrian 1937). By exposing eyes to flickering light and placing electrodes on the scalp, they were able to

record rhythmic potentials at a frequency of up to 25 Hz. By the 1960s, VEPs were starting to become an established neurophysiological test, with their utility being explored as a diagnostic tool for demyelinating disease, tumours compressing the optic pathway, and stroke, amongst other pathologies. It was only a decade later that the technique was employed intra-operatively as a surrogate for the integrity of the visual pathway, particularly for orbital, transsphenoidal, cortical and endoscopic surgery (Sharika, Mirela, and Dinesh 2016) (Anschel 2018) (Singh 2018).

Conclusion

Real-time monitoring of the neural tracts with IONM is invaluable in preventing neurological deficits after surgery, thereby transforming patient outcomes. This chapter has explored the origins of the technique, including major milestones achieved in the monitoring of sensory and motor tracts and other pathways. The unwanted effects of volatile anaesthetic agents on spontaneous and evoked potentials, and the lack of specific equipment, were major obstacles that had to be overcome before the technique could gain traction around the world. The utility of IONM continues to evolve based on the accumulated experience and understanding of surgeons, anaesthetists and neurophysiologists.

References

Adrian, E. D. 1937. “Synchronized reactions in the optic ganglion of dytiscus.” *Journal of Physiology* 91 (1):66-89.

Anschel, D. J. 2018. “Intraoperative Visual Evoked Potentials.” *Journal of Clinical Neurophysiology* 35 (4):355.

Barker, A. T., R. Jalinous, and I. L. Freeston. 1985. “Non-invasive magnetic stimulation of human motor cortex.” *Lancet* 1 (8437):1106-7.

Boyd, S. G., J. C. Rothwell, J. M. Cowan, P. J. Webb, T. Morley, P. Asselman, and C. D. Marsden. 1986. “A method of monitoring function in corticospinal pathways during scoliosis surgery with a note on motor conduction velocities.” *Journal of Neurology, Neurosurgery & Psychiatry* 49 (3):251-7.

Coppola, A., V. Tramontano, F. Basaldella, C. Arcaro, G. Squintani, and F. Sala. 2016. “Intra-operative neurophysiological mapping and monitoring during brain tumour surgery in children: an update.” *Childs Nervous System* 32 (10):1849-59.

Croft, T. J., J. S. Brodkey, and F. E. Nulsen. 1972. “Reversible spinal cord trauma: a model for electrical monitoring of spinal cord function.” *Journal of Neurosurgery* 36 (4):402-6.

Devlin, V. J., and D. M. Schwartz. 2007. “Intraoperative neurophysiologic monitoring during spinal surgery.” *Journal of the American Academy of Orthopaedic Surgeons* 15 (9):549-60.

Fritsch, G., and E. Hitzig. 2009. “Electric excitability of the cerebrum (Uber die elektrische Erregbarkeit des Grosshirns).” *Epilepsy & Behavior* 15 (2):123-30.

Harrington, P.R. 1962. “Treatment of Scoliosis.” *The Journal of Bone and Joint Surgery* 44-A (4):591-634.

Inghilleri, M., A. Berardelli, G. Cruccu, A. Priori, and M. Manfredi. 1990. “Motor potentials evoked by paired cortical stimuli.” *Electroencephalography & Clinical Neurophysiology* 77 (5):382-9.

Iwasaki, H., T. Tamaki, M. Yoshida, M. Ando, H. Yamada, S. Tsutsui, and M. Takami. 2003. “Efficacy and limitations of current methods of intraoperative spinal cord monitoring.” *Journal of Orthopaedic Science* 8 (5):635-42.

Jasper, H. H. 1949. “[The electroencephalography in neuro-surgery].” *Presse Medicale* 57 (63):890.

Jasper, H. H. 1952. “Electroencephalography.” *Pediatrics* 9 (6):786-7.

Jellinek, D., D. Jewkes, and L. Symon. 1991. “Noninvasive intraoperative monitoring of motor evoked potentials under propofol anesthesia: effects of spinal surgery on the amplitude and latency of motor evoked potentials.” *Neurosurgery* 29 (4):551-7.

Jones, S. J., M. A. Edgar, A. O. Ransford, and N. P. Thomas. 1983. “A system for the electrophysiological monitoring of the spinal cord during operations for scoliosis.” *Journal of Bone & Joint Surgery - British Volume* 65 (2):134-9.

Jones, S. J., R. Harrison, K. F. Koh, N. Mendoza, and H. A. Crockard. 1996. “Motor evoked potential monitoring during spinal surgery: responses of distal limb muscles to transcranial cortical stimulation with pulse trains.” *Electroencephalography & Clinical Neurophysiology* 100 (5):375-83.

Kelly, D. L., Jr., S. Goldring, and J. L. O'Leary. 1965. “Averaged Evoked Somatosensory Responses from Exposed Cortex of Man.” *Archives of Neurology* 13:1-9.

Kim, K., C. Cho, M. S. Bang, H. I. Shin, J. H. Phi, and S. K. Kim. 2018. “Intraoperative Neurophysiological Monitoring: A Review of Techniques Used for Brain Tumor Surgery in Children.” *Journal of Korean Neurosurgical Society* 61 (3):363-375.

Koyanagi, I., Y. Iwasaki, T. Isu, H. Abe, M. Akino, and S. Kuroda. 1993. "Spinal cord evoked potential monitoring after spinal cord stimulation during surgery of spinal cord tumors." *Neurosurgery* 33 (3):451-9; discussion 459-60.

Kurokawa, T. 1975. "Proceedings: Clinical application of evoked spinal cord potential measurement." *Electroencephalography & Clinical Neurophysiology* 39 (5):539.

Lesser, R. P., P. Raudzens, H. Luders, M. R. Nuwer, W. D. Goldie, H. H. Morris, 3rd, D. S. Dinner, G. Klem, J. F. Hahn, A. G. Shetter, and et al. 1986. "Postoperative neurological deficits may occur despite unchanged intraoperative somatosensory evoked potentials." *Annals of Neurology* 19 (1):22-5.

Liem, L.K. 2016. Intraoperative Neurophysiological Monitoring. Medscape.

Macdonald, D. B., S. Skinner, J. Shils, C. Yingling, and Monitoring American Society of Neurophysiological. 2013. "Intraoperative motor evoked potential monitoring - a position statement by the American Society of Neurophysiological Monitoring." *Clinical Neurophysiology* 124 (12):2291-316.

Machida, M., S. L. Weinstein, T. Yamada, and J. Kimura. 1985. "Spinal cord monitoring. Electrophysiological measures of sensory and motor function during spinal surgery." *Spine* 10 (5):407-13.

Merton, P. A., and H. B. Morton. 1980. "Stimulation of the cerebral cortex in the intact human subject." *Nature* 285 (5762):227.

Moller, M. B., and A. R. Moller. 1985. "Loss of auditory function in microvascular decompression for hemifacial spasm. Results in 143 consecutive cases." *Journal of Neurosurgery* 63 (1):17-20.

Nash, C. L., Jr., R. A. Lorig, L. A. Schatzinger, and R. H. Brown. 1977. "Spinal cord monitoring during operative treatment of the spine." *Clinical Orthopaedics & Related Research* (126):100-5.

Nuwer, M. R. 2008. "Intraoperative Monitoring of Neural Function." In *Handbook of Clinical Neurophysiology*, edited by Marc Newer, 1-955. New York: Elsevier Ltd.

Nuwer, M. R., E. G. Dawson, L. G. Carlson, L. E. Kanim, and J. E. Sherman. 1995. "Somatosensory evoked potential spinal cord monitoring reduces neurologic deficits after scoliosis surgery: results of a large multicenter survey." *Electroencephalography & Clinical Neurophysiology* 96 (1):6-11.

Patton, H. D., and V. E. Amassian. 1954. "Single and multiple-unit analysis of cortical stage of pyramidal tract activation." *Journal of Neurophysiology* 17 (4):345-63.

Pechstein, U., C. Cedzich, J. Nadstawek, and J. Schramm. 1996. "Transcranial high-frequency repetitive electrical stimulation for recording myogenic motor evoked potentials with the patient under general anesthesia." *Neurosurgery* 39 (2):335-43; discussion 343-4.

Penfield, W., and E. Boldrey. 1937. "Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation." *Brain* 60 (4):389-443.

Sala, F. 2010. "Intraoperative neurophysiology is here to stay." *Childs Nervous System* 26 (4):413-7.

Sharika, R., V.S Mirela, and G.N. Dinesh. 2016. "Intraoperative visual evoked potentials: There is more to it than meets the eye." *J Neurol Neurosci* 7:2-11.

Shimoji, K., H. Higashi, and T. Kano. 1971. "Epidural recording of spinal electrogram in man." *Electroencephalography & Clinical Neurophysiology* 30 (3):236-9.

Singh, L. 2018. "Visual evoked potentials during surgery of the sellar-suprasellar region: The unaddressed issues and the vital caveats." *Neurology India* 66 (4):960-961.

Stecker, M. M. 2012. "A review of intraoperative monitoring for spinal surgery." *Surgical neurology international* 3 (Suppl 3):S174-87.

Tamaki, T., and S. Kubota. 2007. "History of the development of intraoperative spinal cord monitoring." *European Spine Journal* 16 Suppl 2:S140-6.

Tan, T. C., and P. M. Black. 2002. "Sir Victor Horsley (1857-1916): pioneer of neurological surgery." *Neurosurgery* 50 (3):607-11; discussion 611-2.

Taniguchi, M., C. Cedzich, and J. Schramm. 1993. "Modification of cortical stimulation for motor evoked potentials under general anesthesia: technical description." *Neurosurgery* 32 (2):219-26.

Taylor, B. A., M. E. Fennelly, A. Taylor, and J. Farrell. 1993. "Temporal summation--the key to motor evoked potential spinal cord monitoring in humans." *Journal of Neurology, Neurosurgery & Psychiatry* 56 (1):104-6.

Tran, C. T., L. T. Khoo, N. A. Martin, S. S. Fong, and M. R. Nuwer. 2012. "Somatosensory-evoked potential asymmetry in medullary ischemia during cervical spine surgery." *Journal of Clinical Neurophysiology* 29 (1):17-22.

Uematsu, S., R. P. Lesser, and B. Gordon. 1992. "Localization of sensorimotor cortex: the influence of Sherrington and Cushing on the modern concept." *Neurosurgery* 30 (6):904-12; discussion 912-3.

Walker, A. E., H. C. Johnson, and C. Marshall. 1949. "Electrocorticography." *Bulletin of the Johns Hopkins Hospital* 84 (6):583.

Wiedemayer, H., I. E. Sandalcioglu, W. Armbruster, J. Regel, H. Schaefer, and D. Stolke. 2004. "False negative findings in intraoperative SEP monitoring: analysis of 658 consecutive neurosurgical cases and review of published reports." *Journal of Neurology, Neurosurgery & Psychiatry* 75 (2):280-6.

Wing-hay, H.Y., and E.C. Chun-kwong. 2019. "Introduction to Intraoperative Neurophysiological Monitoring for Anaesthetists." World Federation Of Societies of Anaesthesiologists, accessed 21st April 2019. www.wfsahq.org.

CHAPTER 3

NEURO-ANATOMY AND NEUROPHYSIOLOGY

NATALIE SIMON
HAZEL SANGHVI
PRIYA SEKHON
JOHN HANRAHAN
CRISTINA BLEIL

Introduction

To understand the principles of intra-operative neuromonitoring (IONM), it is essential to review the anatomical and physiological principles that underpin its application. The continuous interaction between the peripheral and central nervous systems lends itself to live neurophysiological monitoring but demands that clinicians be familiar with the neural architecture. Such shared knowledge facilitates accurate communication within teams utilising IONM.

This chapter is comprised of a focused review of the relevant systems and processes that govern IONM, which will enable users to understand and apply the technique.

Neurophysiology

The central nervous system operates through electrical signals conducted by nerves. IONM records these electrical signals transmitted through the nervous system in order to monitor function. Thus, maintaining optimal nerve conduction is vital for effective IONM. A range of physiological factors including temperature, pH, electrolyte milieu, perfusion and oxygenation can affect this, as well as drugs – most notably, anaesthetic agents.

Ion channels

The neuronal membrane is a phospholipid bilayer that forms a barrier to water-soluble ions, facilitating a potential difference across the membrane. Changes in this potential difference permit conduction of signals through an axon (Bear, Connors, and Paradiso 2015).

Ion channels are membrane-spanning proteins that allow passive flow of particular ions across the cell membrane. The transmembrane portion of the protein forms the "pore", which determines ion selectivity (Daube 2008). Extracellular or intracellular amino acids of the protein determine the "gating" (opening) and inactivation mechanisms of the channel. Most channels open in response to specific stimuli, such as altered membrane potential (voltage-gated channels), binding of neurotransmitters (ligand-gated channels), or intracellular molecules such as ATP or ions (chemically gated channels) (Daube 2008). Voltage-gated cation channels are responsible for the generation of action potentials and neurotransmitter release within the nervous system. Sodium (Na^+) and potassium (K^+) ion channels maintain the resting membrane potential through tonic leakage of Na^+ inwards and K^+ outwards (Bear, Connors, and Paradiso 2015) (Waxman 2017). This continuous outflow of ions is balanced by the energy-dependent sodium-potassium pump (Na^+/K^+/adenosine triphosphatase [ATPase]), which consumes energy in order to transport ions against their concentration gradients (Daube 2008).

The action potential

Neurones are excitable and respond to stimuli by generating and transmitting electrical impulses. These impulses – modifications of the electrical potential across a membrane – may be local (restricted to the location that received the stimulus) or propagated (travelling along the neurone and its axon) (Waxman 2017). The latter are termed action potentials.

The membrane potential can change in one of two ways: depolarisation, where the membrane potential moves towards zero, with the inside of the cell becoming less negative; and hyperpolarisation, in which the potential moves away from zero, becoming more negative (Bear, Connors, and Paradiso 2015). Responses to electrical, mechanical or chemical stimuli are rapid (of the order of seconds), whereas changes in the concentration of ions are slower and longer-lasting (minutes to hours) (Daube 2008). The generator (receptor) potential is a transient depolarisation or hyperpolarisation

in a localised area of the cell resulting from a change in permeability to one or more ions (Bear, Connors, and Paradiso 2015). This may be in response to a chemical agent, mechanical deformation or applied voltage. Generator potentials are usually depolarising, with opening of both sodium and potassium channels and increasing conductance of both ions (Daube 2008). The magnitude of depolarisation is proportional to that of the stimulus. If a second stimulus is applied before the first subsides, summation of the two occurs and a larger generator potential results (Waxman 2017). Most individual generator potentials are small, with a summated potential being more likely to reach the threshold necessary to produce a propagated action potential in a sensory nerve. This threshold represents the membrane potential at which sufficient numbers of voltage-gated sodium channels open, rendering the ionic permeability of the membrane favourable towards sodium over potassium. This triggers depolarisation, which represents a rush of sodium ions intracellularly. Membrane potential then overshoots, briefly becoming positive. Following this peak, sodium channels close and voltage-gated potassium channels open. An efflux of potassium ions occurs, rendering the membrane potential negative once again; this is repolarisation. As this efflux continues, hyperpolarisation ensues relative to the resting membrane potential, until closure of the potassium channels occurs (Bear, Connors, and Paradiso 2015). An absolute refractory period follows, during which sodium channels cannot be reactivated and so a further action potential cannot be generated. In the subsequent relative refractory period, a stimulus of sufficient magnitude would be able to trigger a second action potential.

The phases of the action potential are summarised in Figure 3-1.

Propagation

For the transfer of information to occur, action potentials must be propagated along the axon. Propagation usually takes place in one direction as the membrane portion just behind it is refractory (Bear, Connors, and Paradiso 2015). The speed – or conduction velocity – at which propagation occurs increases with larger axonal diameter and when a myelin sheath is present. A myelinated axon has breaks, known as nodes of Ranvier, at which the axon is exposed. At these points ions may cross the membrane to generate action potentials, which jump from one node to the next, propagating the action potential rapidly along the nerve in a manner termed saltatory conduction (Bear, Connors, and Paradiso 2015).

Underdeveloped myelination is one reason why IONM is less effective in young infants compared to adults.

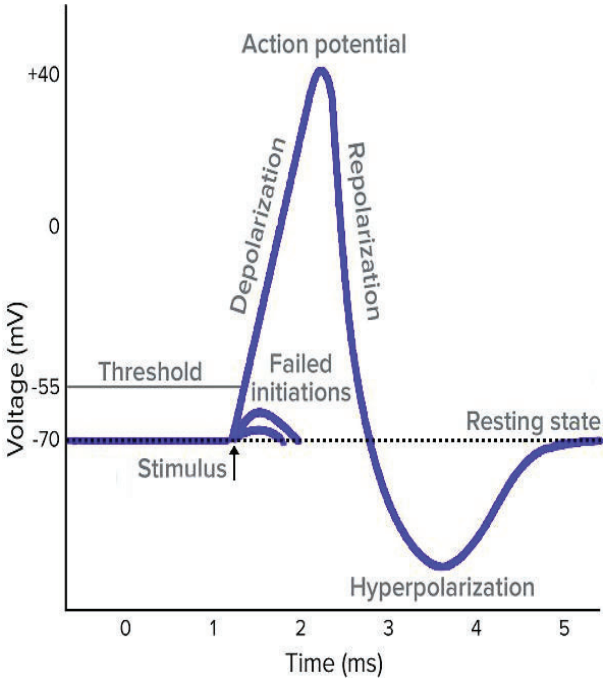

Fig. 3-1. Stages of the action potential.

Synaptic transmission

Neurones communicate with each other at a specialised contact zone, the synapse, by a process called synaptic transmission (Bear, Connors, and Paradiso 2015). Synapses are either excitatory (increasing the probability that the postsynaptic neurone will fire) or inhibitory (reducing this probability). They are also divisible into chemical and electrical, the former being more common. A chemical synapse includes a presynaptic membrane, a synaptic cleft and a postsynaptic membrane. The pre- and postsynaptic components communicate via diffusion of neurotransmitters which are released from vesicles in the presynaptic terminal and bind to postsynaptic receptors (Daube 2008).

Neuroanatomy

Both the sensory and motor functions of the nervous system can be monitored through electrical stimulation and feedback from individual nerves. IONM utilises specific motor and sensory tracts to achieve this aim, the pathways of which are summarised in Figure 3-2.

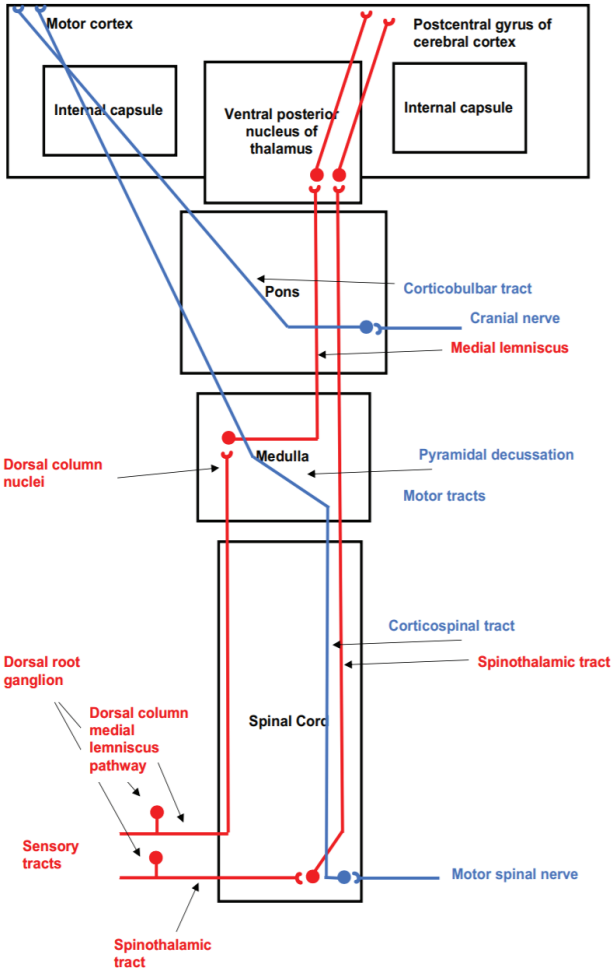

Fig. 3-2. A schematic diagram of the motor (blue) and sensory (red) tracts commonly involved in IONM.

Sensory pathways

The sensory nervous system allows tactile interaction with the environment through several modalities, transmitted via tracts of nerve fibres that originate in the periphery and travel to the central nervous system. These tracts are known as the ascending pathways; the dorsal column-medial lemniscus and spinothalamic tract are the two main conduits (Crossman and Neary 2015). The former is responsible for fine touch, vibration sense, two-point discrimination, and proprioception (Al-Chalabi and Alsalman 2018), whilst the latter confers temperature and pain sensation (lateral spinothalamic tract) and also gross touch and firm pressure (anterior spinothalamic tract) (Al-Chalabi and Gupta 2018). It is the dorsal column medial-lemniscus pathway that is typically monitored during IONM, through the use of somatosensory evoked potentials (SSEPs).

This pathway begins through stimulation of peripheral receptors at sensory nerve endings, which initiates neurotransmission via a series of neurones and synapses. These afferent axons are termed first-order neurones and have nuclei housed in the dorsal root ganglion in the periphery (Crossman and Neary 2015) (Patestas and Gartner 2006). First-order neurones enter the spinal cord via the dorsal root; they ascend ipsilaterally and terminate via synapses in the medulla (Crossman and Neary 2015).

Peripheral nerves originating above the level of T6 synapse with the cuneate nucleus, whilst peripheral nerves arising below this level synapse with the gracile nucleus. The second-order neurone originates in the medulla and decussates before ascending contralaterally in the medial lemniscus (Navarro-Orozco and Bollu 2018). This neurone terminates via a second synapse in the ventral posterolateral nuclei (VPN) of the thalamus. The final, third-order, neurone begins in the VPN and ascends through the internal capsule, where it projects to the sensory cortex (Crossman and Neary 2015). SSEPs utilise the above tracts to record and monitor sensory function intra-operatively.

Motor pathways

There are two major descending motor pathways that are typically monitored intra-operatively: the corticospinal tract and the corticobulbar tract (Sala et al. 2007). The first-order neurones of these tracts arise from the precentral gyrus and the premotor areas of the cerebral cortex (Emos and Agarwal 2018). Corticobulbar tract first-order axons travel from the cerebral cortex and pass through the internal capsule, where they decussate.

Upon reaching the brainstem, these first-order axons synapse onto highly specialised second-order neurones: the cranial nerves (Alpert 2018) (Crossman and Neary 2015). The first-order neurones of the corticospinal tract similarly travel through the internal capsule, but then continue on into the spinal cord (Crossman and Neary 2015). The corticospinal tract is split into lateral and anterior sections; the lateral component contains the vast majority (85-90%) of corticospinal axons and decussates in the medulla, whilst the anterior corticospinal tract contains the remainder of axons and remains ipsilateral (Patestas and Gartner 2006). Eventually these axons reach the spinal cord, where they synapse with second-order neurones which innervate skeletal muscle (Alpert 2018). The lateral corticospinal tracts control somatic limb function, whilst the anterior corticospinal tracts control axial skeletal muscle. Motor evoked potentials (MEPs) monitor the integrity of these tracts during surgery.

Cranial nerves

The twelve cranial nerves differ from spinal nerves by emerging directly from the brain or brainstem. Each has a unique function. They are responsible for the special senses of vision, smell, taste and hearing, as well as balance and other functions of the head and neck. The visual, auditory and vestibular systems are particularly pertinent to IONM and are discussed in detail below. All twelve cranial nerves are summarised in Table 3-1.

Table 3-1. Cranial nerves and respective modes of neuromonitoring. Reproduced with permission (Davis 2014).

Cranial nerve	***Function***	***IONM mode***
Olfactory (I)	Smell	Not monitored
Optic (II)	Vision	Visual evoked potentials
Oculomotor (III)	Eye movement, pupillary constriction and accommodation	EMG of medial/inferior/superior recti, inferior oblique and levator palpebrae muscles
Trochlear (IV)	Eye movement	EMG of superior oblique muscle
b	Ophthalmic, maxillary and mandibular branches provide sensation to the face and motor supply to the muscles of mastication	EMG of temporalis or masseter muscles

Abducens (VI)	Eye movement	EMG of lateral rectus muscle
Facial (VII)	Muscles of facial expression, and stapedius; sensation of the palate, nasopharynx, skin of the outer ear and taste buds of the anterior two thirds of the tongue; autonomic innervation of salivary and lacrimal glands	EMG of orbicularis oculi, orbicularis oris, mentalis and frontalis muscles
Vestibulocochlear (VIII)	Cochlear division (hearing) and vestibular division (equilibrium)	Brainstem auditory evoked potentials
Glossopharyngeal (IX)	Sensory supply to the nasopharynx, oropharynx, middle ear, skin of the outer ear, carotid body and carotid sinus; taste sensation to the posterior one third of the tongue; autonomic supply to the parotid gland; motor supply to stylopharyngeus	EMG of soft palate
Vagus (X)	Sensory supply to the skin of the outer ear, thoraco-abdominal viscera and epiglottal and oesophageal taste buds; autonomic supply and sensation to the larynx and pharynx	EMG of pharyngeal and laryngeal muscles supplied by recurrent laryngeal nerve
Spinal accessory (XI)	Motor supply to sternocleidomastoid and trapezius	EMG of sternocleidomastoid and trapezius muscles
Hypoglossal (XII)	Muscles of the tongue	EMG of tongue

Visual pathway

The visual pathway is a continuous connection of nerve fibres beginning in the ganglion cells of the innermost retinal layer. The axons of these cells meet at the optic disc and pass through the lamina cribosa, forming the optic nerve head. The optic nerve itself is divided into three anatomical regions: intra-orbital, intracanalicular and intracranial (De Moraes 2013).

Within the intra-orbital region, the optic nerve becomes invested with the meninges and travels posteromedially through the optic canal to become the intracanalicular portion. Upon leaving the optic canal, the now intracranial optic nerve travels posteromedially to the optic chiasm, where it meets its contralateral counterpart. Here, the nerve fibres originating from the nasal retinal layer decussate to join the temporal fibres of the contralateral eye, and travel posteriorly to the lateral geniculate nucleus as the optic tract.

The lateral geniculate nucleus, located within the thalamus, contains the second neurone of the visual pathway and is organised into six layers. Layers 1, 4 and 6 synapse with the nasal fibres from the contralateral eye, while the temporal fibres from the ipsilateral eye synapse in layers 2, 3 and 5 (Wichmann and Muller-Forell 2004). In addition to the optic tract, the lateral geniculate nucleus receives neuronal input from the visual cortex and the thalamic reticular and pulvinar nuclei (De Moraes 2013). Neurones arising from the lateral geniculate nucleus traverse the optic radiations that initially project anteriorly before turning posterolaterally, passing across the lateral ventricle to the visual cortex. The nerve fibres synapse in the primary visual cortex (V1), which occupies the calcarine fissure of the occipital lobe (Wichmann and Muller-Forell 2004). This area represents the horizontal meridian of the visual field, whereas the vertical meridian lies in within the calcarine lips; the central field is depicted in the posterior pole of the occipital cortex. Visual processing is further modulated by up-down connections between thalamic and other cortical areas to allow interpretation of visual signals (De Moraes 2013). Visual evoked potentials (VEPs) test the integrity of these tracts using an eye flash stimulator.

Auditory pathway

The auditory system enables hearing and provides the sensory input necessary for speech recognition. Sound waves converge through the pinna and outer ear canal to strike the tympanic membrane, from which vibrations are transmitted via the ossicles (malleus, incus and stapes) of the middle ear, to the oval window (Bear, Connors, and Paradiso 2015). This motion in turn moves fluid within the cochlea of the inner ear. The cochlea is a portion of membranous labyrinth within the temporal bone of the skull base and is the specialised organ that registers and transduces sound waves. The auditory receptors, known as hair cells, convert mechanical stimuli into electrical signals. Hair cells form synapses with neurones whose cell bodies are located in the spiral ganglion. Afferent

nerves then enter the brainstem as the auditory vestibular nerve (cranial nerve VIII). The axons innervate the dorsal and ventral cochlear nuclei at the level of the ipsilateral medulla. Each axon branches to synapse on neurones in both cochlear nuclei. From the ventral cochlear nucleus, axons project to the superior olive (also known as the superior olivary nucleus) on both sides of the brainstem. Axons from the olivary nucleus ascend in the lateral lemniscus and innervate the inferior colliculus of the midbrain. The axons from the dorsal cochlear nucleus follow a similar route but bypass the superior olive. All ascending auditory pathways converge onto the inferior colliculus, which projects axons to the medial geniculate nucleus of the thalamus; this in turn projects to the auditory cortex (Bear, Connors, and Paradiso 2015) (Waxman 2017). The auditory pathway is illustrated in Figure 3-3.

The vestibulocochlear nerve and brainstem auditory pathways are at particular risk of damage during surgery involving the cerebellopontine angle, posterior or middle fossae, or brainstem. Injury may be sustained through vascular compromise, thermal or mechanical stress, or damage to the cochlea. The auditory function of the vestibulocochlear nerve can be monitored using brainstem auditory evoked potentials (BAEPs) (Simon 2011) (Emerson and Adams 2012). These are a series of waves generated within auditory structures in the brainstem in response to auditory stimuli. They reflect the integrity of the auditory component of the vestibulocochlear nerve, but not the vestibular system.

Vestibular system

The vestibular system monitors the position and movement of the head, conferring our sense of balance and equilibrium. It permits co-ordinated movements of the head and eyes, and assists with maintenance of body posture (Waxman 2017). In addition to the structures of the auditory system, the membranous labyrinth also contains the otolith organs, which detect gravitational force and tilt, and the semi-circular canals, which are sensitive to head rotation (Bear, Connors, and Paradiso 2015). These structures transmit mechanical energy to the hair cells, which synapse with sensory axons of the vestibular nerve. From here, connections are made to the vestibular nucleus on the ipsilateral brainstem, and to the cerebellum. Projections from the vestibular nuclei reach the cerebellum, ipsilateral spinal cord (via the lateral vestibulospinal tracts), nuclei of the eye muscles, and the motor nuclei of the upper spinal nerves (via the medial longitudinal fasciculi) (Waxman 2017). In keeping with other sensory systems, connections are made with the thalamus (at the ventral posterior

nucleus) and then to the primary somatosensory and primary motor areas of the cortex (Bear, Connors, and Paradiso 2015) (Waxman 2017).

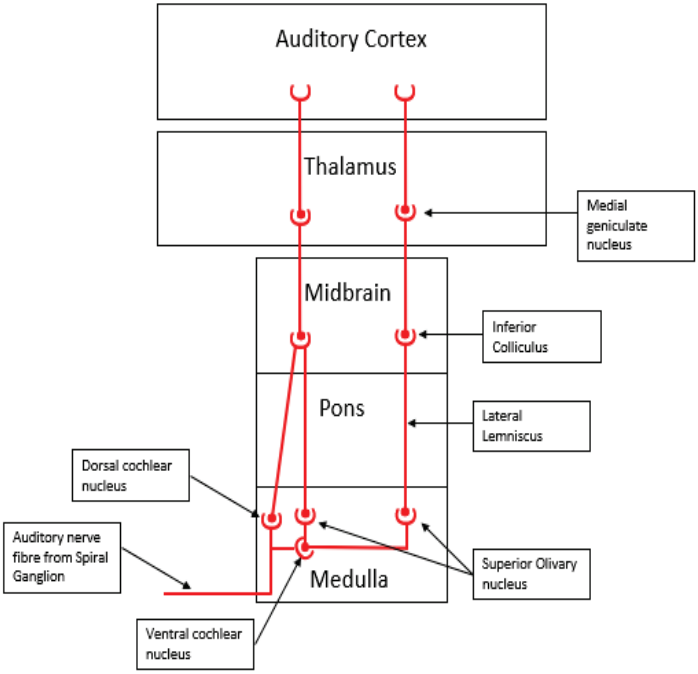

Fig. 3-3. Auditory pathway.

References

Al-Chalabi, M., and I. Alsalman. 2018. "Neuroanatomy, Posterior Column (Dorsal Column)." *StatPearls Publishing* 01:01.

Al-Chalabi, M., and S. Gupta. 2018. "Neuroanatomy, Spinothalamic Tract." *StatPearls Publishing* 01:01.

Alpert, J.N. 2018. "The Six Major Anatomic Decussations with Clinical Correlation. In: The Neurologic Diagnosis." In *The Neurologic Diagnosis*, edited by J.N. Alper, 207-227. Springer Nature Switzerland: Springer, Cham.

Bear, M.F, B.W. Connors, and M.A. Paradiso. 2015. "Exploring the brain." In *Neuroscience*, 331-368. Lippincott Williams & Wilkins.

Crossman, A.R., and D. Neary. 2015. *Neuroanatomy: an illustrated colour text*. New York: Churchill Livingstone Elsevier.

Daube, J.R. 2008. "Physiology." In *Intraoperative Monitoring of Neural Function*, edited by M.R. Nuwer, 7-43. Elsevier Ltd.

Davis, S.F. 2014. " Anatomy of Intraoperative Monitoring " In *Principles of Neurophysiological Assessment, Mapping, and Monitoring* edited by A.D. Kaye and S.F. Davis, 11-46. New York: Springer

De Moraes, C. G. 2013. "Anatomy of the visual pathways." *Journal of Glaucoma* 22 Suppl 5:S2-7.

Emerson, R.G., and D.C. Adams. 2012. "Intraoperative monitoring by evoked potential techniques." In *Aminoff's Electrodiagnosis in Clinical Neurology*, 651-670. United States: Elsevier Inc.

Emos, M. C., and S. Agarwal. 2018. "Neuroanatomy, Upper Motor Neuron Lesion." *StatPearls Publishing* 01:01.

Navarro-Orozco, D., and P. C. Bollu. 2018. "Neuroanatomy, Medial Lemniscus (Reils Band, Reils Ribbon)." *StatPearls Publishing* 01:01.

Patestas, M.A., and L.P. Gartner. 2006. *A Textbook of Neuroanatomy*: Blackwell Publishing

Sala, F., P. Manganotti, V. Tramontano, A. Bricolo, and M. Gerosa. 2007. "Monitoring of motor pathways during brain stem surgery: what we have achieved and what we still miss?" *Neurophysiologie Clinique* 37 (6):399-406.

Simon, M. V. 2011. "Neurophysiologic intraoperative monitoring of the vestibulocochlear nerve." *Journal of Clinical Neurophysiology* 28 (6):566-81.

Waxman, S.G. 2017. *Clinical neuroanatomy*. 28 ed. New York: McGraw.

Wichmann, W., and W. Muller-Forell. 2004. "Anatomy of the visual system." *European Journal of Radiology* 49 (1):8-30.

CHAPTER 4

BRAIN MAPPING: NEUROPHYSIOLOGISTS' PERSPECTIVE

NOEMIA PEREIRA
HANNAH KEEBLE

Introduction

Intra-operative mapping and monitoring during the resection of supratentorial brain tumours permits a more aggressive surgical approach; this maximises tumour resection (Ciric et al. 1987) whilst preserving neurological function (Rossi et al. 2019), and consequently improves patients' quality of life (Kombos, Suess, and Brock 2000). This chapter discusses how and why intra-operative neurophysiology is utilised in supratentorial neurosurgical procedures. We provide a brief chronological overview of brain mapping and monitoring techniques, and discuss the current intra-operative neurophysiological protocols used for cortical and subcortical mapping of eloquent brain.

Penfield and Boldrey were some of the first to publish on the use of electrical stimulation of the cortex of awake patients to evoke motor responses (Penfield and Boldrey 1937). This is now considered a landmark publication that defined human cortical organisation of motor and sensory function; this was later published as a map, as illustrated in Figure 4-1 (Penfied and Rasmussen 1950). Penfield's low frequency technique for brain mapping stimulation is still frequently used in awake patients as a means of assessing function around the area of surgical resection (Kombos, Suess, and Brock 2000). A major disadvantage in the early use of this technique was the high incidence of seizure activity following stimulation in the non-anaesthetised patient. This was particularly problematic during

microsurgery and long procedures, as it precluded continuous monitoring of motor function (Kombos, Suess, and Brock 2000) (Yingling 2011). In 1993, Taniguchi et al described a modified method of cortical motor stimulation using a high-frequency multi-pulse train in anaesthetised patients (Taniguchi, Cedzich, and Schramm 1993). This adaptation evoked minimal movement and seizure activity, allowing continuous monitoring throughout surgery (Kombos, Suess, and Brock 2000). The technique permits objective analyses of evoked muscle responses, and is now frequently used in the resection of tumours close to eloquent motor areas (Rossi et al. 2019).

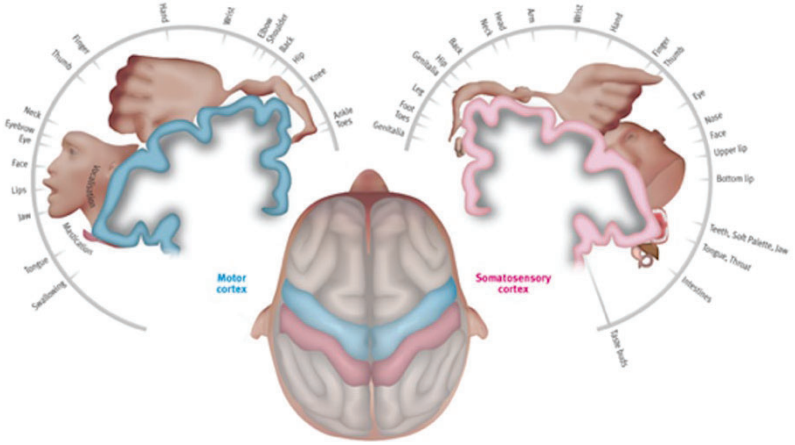

Fig. 4-1. Homunculi maps. The left image represents the motor homunculus, and the right, the sensory homunculus. Adapted with permission (inomed GmbH, adapted from Penfield and Rasmussen 1950).

Knowledge of the cortical anatomy, vascular supply, and subcortical white matter tracts of the brain, along with the effects of anaesthesia, is crucial to understand which functions are at risk and to plan monitoring accordingly. The primary motor and sensory cortices are typically defined as the regions encompassing the precentral and postcentral gyri (Gogtay et al. 2004), corresponding to Brodmann's cytoarchitectural areas 4 and 1, 2, and 3, respectively (Brodmann 1909). During supratentorial tumour resections, the cortical upper motor neurone pyramidal cells and subcortical white matter axonal tracts are monitored and mapped. The monitoring comprises the continuous stimulation and recording of either somatosensory and/or motor function. This allows continuous assessment of the entire afferent and efferent tracts to ensure that these pathways remain intact throughout a

procedure. Mapping refers to an active search with a stimulation probe, either cortically or subcortically, to locate eloquent regions and provide warnings of surgical proximity to them (Seidel et al. 2013). The goal of the functional mapping tool is to define the boundaries between functional areas and non-functional tumour tissue (Günel, Piepmeier, and Baehring 2016) in order to facilitate precise tumour resection whilst retaining functional integrity (Sala and Lanteri 2003).

For supratentorial procedures, a range of methods are used to reliably identify and preserve functional tissue, including transcranial magnetic stimulation (TMS), intra-operative MRI, and diffusion tensor imaging (DTI) tractography. These techniques are commonly used together to further the specificity of tumour resection. Pre-operative TMS uses non-invasive magnetic fields to deliver electrical pulses to the brain in order to map the motor and speech regions; DTI allows the surgeon to pre-operatively identify the course of subcortical tracts in a pre-operative MRI, providing a three-dimensional reconstruction of the white matter bundles. These technologies are helpful for pre-operative planning and identification of structures at risk of iatrogenic damage, as well as for intra-operative guidance when integrated into multimodal neuro-navigation systems. However, once surgery has begun, the pre-operative MRI data upon which these technologies rely become less accurate as the natural anatomy is disturbed. This is why intra-operative neuromonitoring is crucial, as it provides continuous feedback on tissue functionality (Duffau 2008).

Sensory mapping

Somatosensory evoked potentials (SSEPs)

SSEPs are obtained by stimulation of peripheral nerves, the most common being the median nerve for the upper limb (or ulnar nerve, if an arterial line is present), and the posterior tibial nerve for the lower limb. Subdermal needles (such as inomed GmbH, 15-20 mm length) are used with a constant current stimulator (such as ISIS Neurostimulator, inomed GmbH). The electrical stimulus is a positive waveform pulse of 0.2-0.5 ms, delivered at a frequency of 3.1 to 5.1 Hz, administered on average 50-200 times. The current intensity is increased until thumb/foot muscle twitches are observed, up to a maximum of 50 mA. Mean evoked potential traces are obtained by averaging the electrophysiological signals time-locked to the stimulation. Cortical SSEPs are recorded by subdermal corkscrew needles (such as inomed GmbH, 0.6 mm length) positioned in the postcentral parietal regions bilaterally, in addition to the midline (C3, C4, Cz, Fz), according to the 10-

20 International Electrode System (Sinha et al. 2016) (Acharya et al. 2016). Corkscrew electrodes may be positioned in more posterior locations according to the craniotomy location; however, this should not affect the responses. Needles are also placed to record the peripheral responses at the right and left Erb's points (for upper limb) and popliteal fossae (for lower limb), as well as at the brainstem level (CV2) (Figure 4-2).

SSEPs in supratentorial procedures are mainly used to detect changes related to cerebral blood flow, which may be diminished by vascular injury during tumour resection. SSEPs arising from the median and posterior tibial nerves are used to monitor the middle cerebral artery (MCA) and the anterior cerebral artery (ACA) respectively. The MCA supplies the lateral primary sensory cortex and subcortical sensory fibres of the upper limb. The ACA supplies the mesial primary sensory cortex and subcortical sensory fibres of the lower limb. A partial cortical ischaemic event can cause single SSEP decrement. A decrease in both upper and lower limb SSEPs may indicate ischaemia of deeper structures, such as the lenticulostriate branches of the middle cerebral arteries and branches of the anterior choroidal arteries, which supply thalamocortical sensory axons. Thalamic sensory nuclei are supplied by posterior cerebral artery branches; the medial lemniscus is fed by basilar and vertebral artery branches. SSEPs can also be useful in detecting disruption of the somatosensory network within tumours invading the postcentral gyrus (Jahangiri et al. 2020).

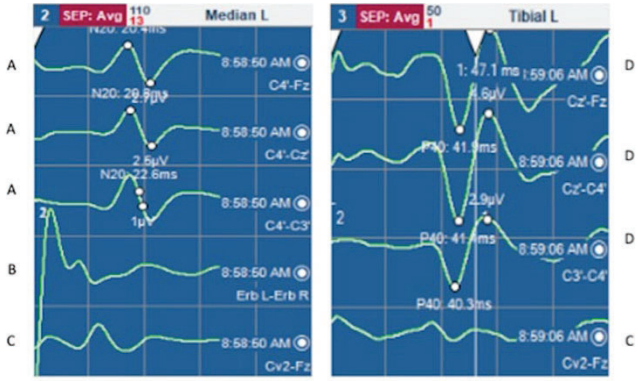

Fig. 4-2. SSEP responses at baseline. A: Left median nerve responses (N20 waveforms). B: Left Erb's point peripheral response. C: Brainstem response. D: Left posterior tibial nerve responses (P40 waveforms).

Phase reversal

Traditionally, functional mapping begins with the accurate identification of the central sulcus, which subsequently identifies the pre- and postcentral gyri – primary motor and sensory cortices – using the technique known as phase reversal (Yingling 2011) (Jahangiri et al. 2020) (Cedzich et al. 1996). This is performed by stimulation of the peripheral nerves contralateral to the exposed cortical hemisphere, similarly to SSEPs, and recording through a subdural grid or strip electrode of between four and eight contacts. This electrode is placed under the dura or onto the exposed cortex, in a perpendicular position over the central sulcus (Figure 4-3). When positioned over the somatotopic hand area, the contralateral median (or ulnar) nerve is stimulated. For more mesial exposure towards the inter-hemispheric fissure (somatotopic leg area), the contralateral posterior tibial nerve may be used. A reversal in polarity of the N20-median or P40-posterior tibial thalamocortical SSEP responses is observed approximately 20 ms after stimulation of the contralateral nerves (Figure 4-4). This indicates the location of the central sulcus as lying between the two contacts with differing inverting polarity electronegative potentials (Kombos, Suess, and Brock 2000) (Jahangiri et al. 2020).

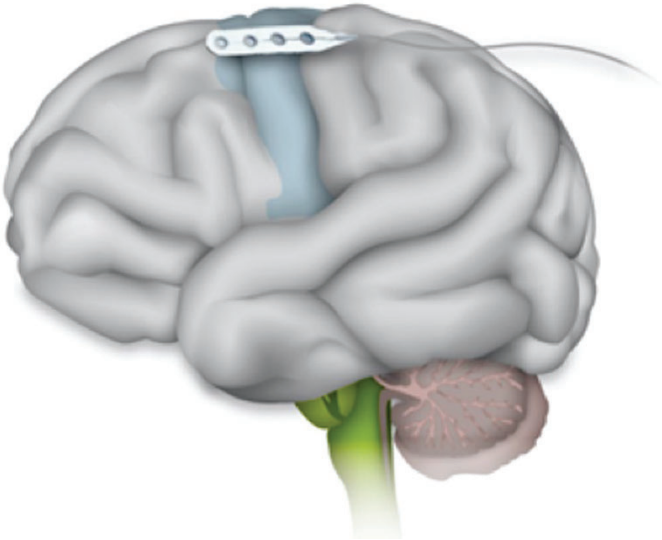

Fig. 4-3. Placement of the four-contact cortical strip electrode perpendicular to the central sulcus, covering both the pre-central and postcentral gyri.

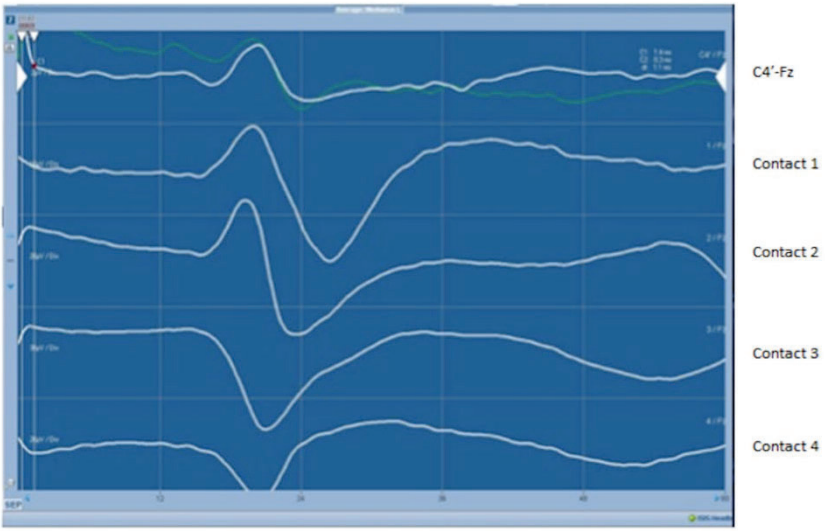

Fig. 4-4. Median nerve SSEP phase reversal technique using a four-contact strip electrode, with a reference electrode on the contralateral mastoid (Fz). Phase reversal is observed between contacts 2 and 3. The electronegative potentials seen at contact 1 and 2 represent the N20 thalamocortical potential obtained in the postcentral somatosensory cortex. Scalp SSEPs, displayed on the top waveform (C4'-Fz, N20), help to distinguish somatosensory responses from motor responses.

Motor mapping

Paradigm of stimulation

The primary motor areas can be identified in awake patients or under general anaesthesia by direct electrical stimulation. As mentioned earlier in this chapter, the first method described in awake human patients consisted of applying long trains (1-6 s) of biphasic pulses at low frequency (50-60 Hz) until a movement was elicited (Figure 4-5) (Penfield and Boldrey 1937). More recently, a train-of-five multi-pulse, high-frequency technique was introduced with several advantages over the original Penfield method, including objective analysis of evoked muscle responses in the anaesthetised patient, and the ability to continuously monitor (Bello et al. 2014). The train-of-five technique delivers short trains of five, anodal or cathodal, monophasic, square-wave pulses of high frequency (250-500 Hz), with a low train repetition rate (1 Hz) (Figure 4-6).

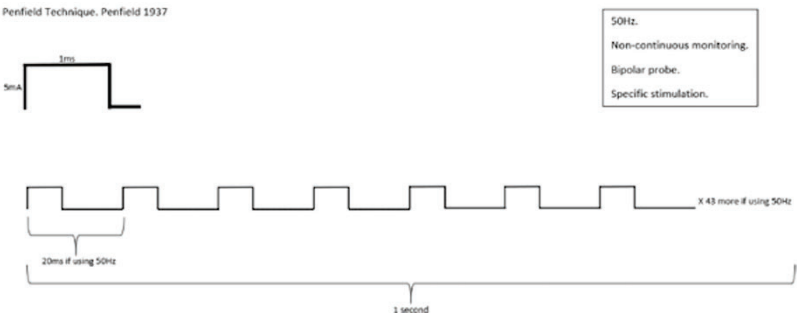

Fig. 4-5. A visual representation of the Penfield technique.

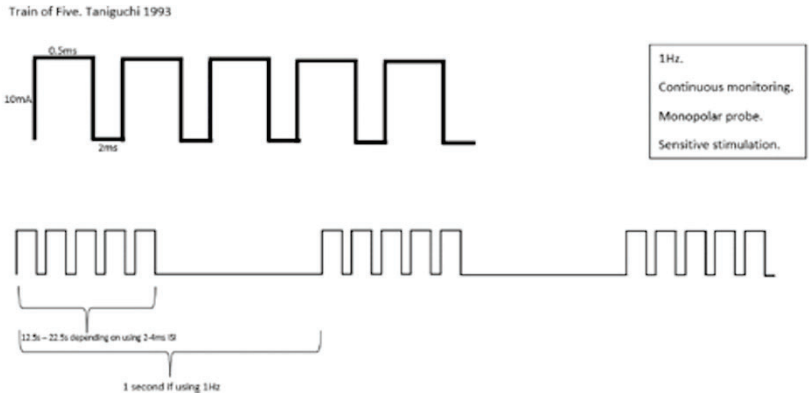

Fig. 4-6. A visual representation of the train-of-five technique.

Supratentorial motor stimulation can be performed using both techniques with either a monopolar or bipolar probe. Monopolar stimulation provides a radiant spreading of the electric field, reaching more distant sites and providing "sensitive" mapping. In bipolar stimulation, the peak current density occurs in the region immediately beneath the bipolar probe and it reduces rapidly thereafter, providing more "specific" mapping (Szelényi and Bello 2010). A monopolar probe combined with the train-of-five technique is most often used for mapping of the motor cortex in anaesthetised patients, since it requires the lowest current intensity to reproduce an MEP compared to any other combination of stimulation and probe (Szelenyi et al. 2011). This reduces the incidence of seizures and is much more successful in the paediatric population compared to the Penfield technique (Roth et al. 2020); it also overcomes difficulties associated with anatomical distortion (Rossi et al. 2019).

MEPs are recorded using paired subdermal needles placed into the chosen group of muscles according to the tumour location. A broad representation of the motor cortex somatotopy is required in order to safely preserve eloquent motor cortex and corticospinal tract (CST) subcortically. A single muscle representation of the ipsilateral upper and lower limbs serve as technical controls. Specific muscles are preferred for differing region. Facial representation is obtained via orbicularis oris, the tongue, masseter, and cricothyroid muscles. For the upper limb, deltoid, biceps, triceps, brachioradialis, flexor carpi ulnaris, the first dorsal interosseous, abductor digiti minimi, and the abductor pollicis brevis are preferred. In the lower limb, quadriceps, anterior tibialis, gastrocnemius, and the abductor hallucis are used. Differing muscles and combinations are possible; a recent publication by Ghimire et al. demonstrated the use of intercostal muscle representation cortically and subcortically in order to resect a glioma (Ghimire et al. 2019).

Cortical motor mapping and monitoring

Direct cortical stimulation can be used to map the motor cortex in order to identify functional areas to be avoided by corticotomy. It may be applied to the primary motor cortex using a monopolar or bipolar probe (Kombos, Suess, and Brock 2000); the former is often preferred. The train-of-five technique is used, as this provides a homogeneous radiant spreading electric field, increasing the probability of stimulating surrounding functional tissue; this confers higher sensitivity and a reduced risk of provoking epileptogenic activity (Bello et al. 2014) (Kombos et al. 1999). The motor threshold is measured, which corresponds to the lowest stimulus intensity that reproduces a replicable MEP ($\geq$200 mV). Following motor mapping, a suprathreshold stimulus is applied to the vicinity of the planned resection to identify the safest point of entry. The stimulation comprises a train of three to five constant-current, anodal pulses (pulse width 0.5 ms; interstimulation interval (ISI) 2-4 ms) at a repetition rate of 1 Hz (Taniguchi, Cedzich, and Schramm 1993) and a maximum current intensity of 25 mA (Nathan et al. 1993). The ISI can be modified according to the cortical area being mapped; for the face and upper limb, an ISI of 2 ms is optimal, whilst for lower limb an ISI of 4 ms seems to provide more stable readings. The pulse duration may be increased to 0.8 ms in patients with a high motor threshold (Bello et al. 2014).

After identifying the precentral gyrus using the phase reversal technique or direct cortical stimulation, a strip electrode is positioned in line with the motor cortex and used to stimulate MEPs using the train-of-five stimulation

in both awake and anaesthetised patients. Each electrode contact is tested against a reference electrode on the scalp, allowing monitoring of the integrity of the CST (Sala and Lanteri 2003) (Neuloh et al. 2004). Ideally, the strip electrode should be continuously evoking responses from muscles which are somatotopically represented in the motor cortex closest to, or disrupted by, the lesion to be resected. For example, if a tumour is located in the posterior superior frontal gyrus, the leg and foot area are of most concern; therefore the strip electrode should be covering that cortical region. Stimulation of the strip electrode occurs throughout the procedure (Seidel et al. 2013), at 30-60 second intervals, to reduce the risk of provoking a seizure. With large tumours, often the strip electrode and/or brain tissue shift from their baseline positions, and a false-positive loss of MEPs occurs. Because of this, intra-operative readjustment of the strip may be required.

Subcortical motor mapping

Subcortical stimulation for motor mapping is currently considered the gold standard for locating white matter fibres (Seidel et al. 2013) (Szelenyi et al. 2011) (Raabe et al. 2014). It is possible to identify the surgeon's real-time distance to the white matter tracts, dependent on the stimulation intensity and the MEP response motor threshold: 1 mA approximates to a 1 mm distance (Seidel et al. 2020). In neuro-oncology, maximising the extent of tumour resection is key to improve survival, but avoiding postoperative deficits is also paramount to maintain quality of life. An electrically-isolated standard suction device with monopolar capability, connected to a neuromonitoring device (Figure 4-7) allows the use of continuous stimulation where the tip of the suction device is directed. The stimulation parameters are identical to those of classical subcortical mapping: cathodal stimulation using the train-of-five technique at a 1 Hz repetition rate, with 0.5 ms pulse width, 2-4 ms ISI, and using a constant current stimulator (e.g. ISIS Xpress System, inomed GmbH) (Szelenyi, Joksimovic, and Seifert 2007) (Deletis, Isgum, and Amassian 2001) (Deletis, Rodi, and Amassian 2001). The dynamic monopolar suction probe enables the surgeon to continuously yet unobtrusively map the CST. This has recently been demonstrated a feasible and safe technique for localising the exact site of the CST and distance to the motor fibres (Seidel et al. 2020).

A current intensity of 10 mA is initially used, and, after a motor response is detected suggesting a distance of 10 mm from the corticospinal tract, 2 mA reductions are employed in a stepwise resection as the corticospinal tract is approached, down to 3-5 mA. Whilst subcortical mapping is in process,

cortical MEPs are periodically monitored through the strip electrode, ensuring the integrity of the entire tract.

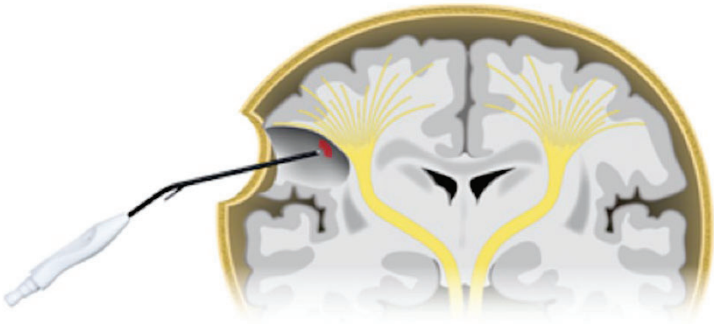

Fig. 4-7. Subcortical stimulation using the inomed Raabe Monopolar suction probe to determine the real-time distance to the corticospinal tracts.

Cortical MEPs and SSEPs should be utilised in parallel to detect changes related to cerebral blood flow, which may be caused by vascular injury. This is because the sensory and motor cortices share the same blood supply (Chen et al, 2004); therefore an amplitude drop in MEPs and SSEPs in response to an ischaemic event can predict the motor function of the patient postoperatively (Thirumala et al. 2013) (MacDonald et al. 2019).

Speech mapping

Awake procedures

"Awake" surgery (in which patients are awakened intra-operatively) is currently the gold standard for intra-operative testing of speech and language (Szelényi and Bello 2010). When direct electrical stimulation is applied to the cortical and subcortical structures essential for speech, a patient may be temporarily rendered unable to speak (general speech arrest). Speech and language therapists carry out different tests with the patient intra-operatively, whilst the operating surgeon stimulates different locations with a bipolar fork probe. The tasks asked of the patient are specific to the location of their individual lesion and may include: number-counting; picture-naming tasks such as the Boston naming test (LaBarge, Edwards, and Knesevich 1986) (Talacchi et al. 2013); repetition; sentence completion; and many others. Besides general speech arrest, changes that may occur include paraphasia, dysarthria and other functional variations

(Talacchi et al. 2013). Speech and language are not the only functions tested during awake procedures; higher cognitive skills, fine motor movements, sensation, and vision can all be examined.

For awake functional mapping, the Penfield stimulation technique is employed using a bipolar probe (with 2 mm diameter ball tips, spaced 5 mm apart, inomed GmbH) to elicit biphasic square-wave pulses of 1 ms duration, applied at a frequency of 50-60 Hz, for 5-8 s using a constant current stimulator (e.g. ISIS Neurostimulator, inomed GmbH). The current commences at 2 mA and the threshold is set at the minimal current to evoke functional errors without triggering after-discharges in the electrocorticography (ECoG); this may be increased in 1-2 mA increments, up to 6 mA. To distinguish motor arrest from speech arrest, free-running EMG recordings are also monitored.

Electro-encephalography and electrocorticography

The major drawback of conventional Penfield stimulation in awake patients is the high incidence of intra-operative seizures induced by prolonged stimulation (Zangaladze et al. 2008). In supratentorial surgery, free-running electro-encephalography (EEG) and electrocorticography (ECoG) are used to monitor depth of anaesthesia (Musizza and Ribaric 2010) and potential seizure activity. EEG is recorded by subdermal corkscrew needles positioned on the scalp bilaterally, while ECoG is monitored via a strip electrode placed over the exposed brain proximal to the stimulation site. Electrodes are referenced against each other as well as a midfrontal scalp subdermal corkscrew (Figure 4-8). EEG and ECoG recordings are filtered (bandpass 0.5-100 Hz), running at a sensitivity of 30 mm sec^{-1}. The major advantage of ECoG over EEG is that it attracts less dispersion and attenuation of potentials due to absence of scalp and skull; it also detects after-discharge activity in the absence of physical signs of seizures (i.e., subclinical or non-convulsive seizure activity).

Whether either EEG or ECoG is in use, the recording should be constantly monitored. If after-discharges are observed, the surgical team should be alerted, and cold irrigation must be applied to the brain immediately. This will rapidly suppress the activity and avoid progression to clinical seizures, which can be extremely challenging to manage and place the patient in danger (Hervey-Jumper et al. 2015) (Formaggio et al. 2013). Free-running EMG is continuously recorded alongside the EEG and/or ECoG, which confers early detection of spreading muscle activation indicative of seizure activity (Szelényi and Bello 2010).

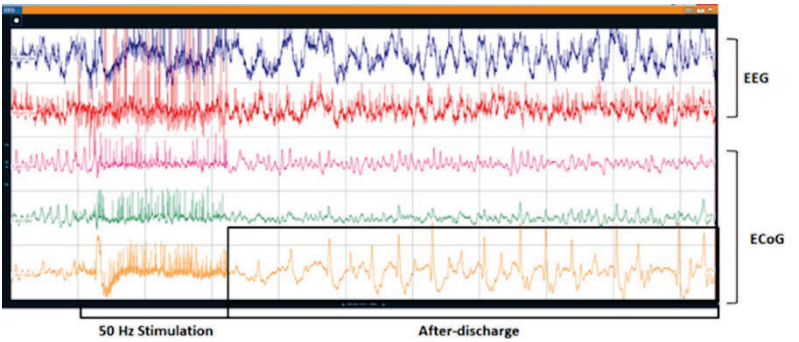

Fig. 4-8. EEG and ECoG recordings during speech and language mapping in an awake patient. After-discharges were recorded from one of the recording channels of a grid electrode placed over the cortex after brain stimulation.

Conclusion

The commonly-used techniques for supratentorial mapping and monitoring have been described in this chapter. The gold standard for preserving function in these procedures is awake mapping; however, this is not suitable or desirable in all patients. IONM provides real-time information on the location and integrity of eloquent anatomy during supratentorial procedures, especially when other navigation systems become less accurate. The expanding role of IONM, especially in multimodal strategies, is fundamental to achieving the best outcomes for neurosurgical patients.

References

Acharya, J. N., A. Hani, J. Cheek, P. Thirumala, and T. N. Tsuchida. 2016. "American Clinical Neurophysiology Society Guideline 2: Guidelines for Standard Electrode Position Nomenclature." *J Clin Neurophysiol* 33 (4):308-11. doi: 10.1097/WNP.0000000000000316.

Bello, L., M. Riva, E. Fava, V. Ferpozzi, A. Castellano, F. Raneri, F. Pessina, A. Bizzi, A. Falini, and G. Cerri. 2014. "Tailoring neurophysiological strategies with clinical context enhances resection and safety and expands indications in gliomas involving motor pathways." *Neuro-Oncology* 16 (8):1110-28.

Brodmann, K. 1909. *Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues*. Leipzig: JA Barth.

Cedzich, C., M. Taniguchi, S. Schafer, and J. Schramm. 1996. "Somatosensory evoked potential phase reversal and direct motor cortex stimulation during surgery in and around the central region." *Neurosurgery* 38 (5):962-70.

Ciric, I., M. Ammirati, N. Vick, and M. Mikhael. 1987. "Supratentorial gliomas: surgical considerations and immediate postoperative results. Gross total resection versus partial resection." *Neurosurgery* 21 (1):21-6.

Deletis, V., V. Isgum, and V. E. Amassian. 2001. "Neurophysiological mechanisms underlying motor evoked potentials in anesthetized humans. Part 1. Recovery time of corticospinal tract direct waves elicited by pairs of transcranial electrical stimuli." *Clinical Neurophysiology* 112 (3):438-44.

Deletis, V., Z. Rodi, and V. E. Amassian. 2001. "Neurophysiological mechanisms underlying motor evoked potentials in anesthetized humans. Part 2. Relationship between epidurally and muscle recorded MEPs in man." *Clinical Neurophysiology* 112 (3):445-52.

Duffau, H. 2008. "Intraoperative neurophysiology during surgery for cerebral tumors." In *Handbook of Clinical Neurophysiology*, 491-507. Elsevier.

Formaggio, E., S. F. Storti, V. Tramontano, A. Casarin, A. Bertoldo, A. Fiaschi, A. Talacchi, F. Sala, G. M. Toffolo, and P. Manganotti. 2013. "Frequency and time-frequency analysis of intraoperative ECoG during awake brain stimulation." *Front Neuroeng* 6:1. doi: 10.3389/fneng.2013.00001.

Ghimire, P., N. Bedussa, A. Giamouriadis, C. Brogna, N. Pereira, H. Howells, R. Bhangoo, K. Ashkan, and F. Vergani. 2019. "Somatotopy of corticospinal tract fibres of the intercostal muscles: report of a case and review of literature." *Brain Structure & Function* 224 (2):515-520.

Gogtay, N., J. N. Giedd, L. Lusk, K. M. Hayashi, D. Greenstein, A. C. Vaituzis, T. F. Nugent, 3rd, D. H. Herman, L. S. Clasen, A. W. Toga, J. L. Rapoport, and P. M. Thompson. 2004. "Dynamic mapping of human cortical development during childhood through early adulthood." *Proc Natl Acad Sci U S A* 101 (21):8174-9. doi: 10.1073/pnas.0402680101.

Günel, J.M., J Piepmeier, M., and J.M Baehring. 2016. *Malignant Brain Tumors: State-of-the-Art Treatment*. USA: Spinger.

Hervey-Jumper, S. L., J. Li, D. Lau, A. M. Molinaro, D. W. Perry, L. Meng, and M. S. Berger. 2015. "Awake craniotomy to maximize glioma resection: methods and technical nuances over a 27-year period." *J Neurosurg* 123 (2):325-39. doi: 10.3171/2014.10.JNS141520.

Jahangiri, F. R., K. Pautler, K. Watters, S. S. Anjum, and G. L. Bennett. 2020. "Mapping of the Somatosensory Cortex." *Cureus* 12 (3):e7332. doi: 10.7759/cureus.7332.

Kombos, T., O. Suess, and M. Brock. 2000. "Intraoperative functional mapping of the motor cortex: A review." *Neurosurgery Quarterly* 10 (4):311-315.

Kombos, T., O. Suess, B. C. Kern, T. Funk, T. Hoell, O. Kopetsch, and M. Brock. 1999. "Comparison between monopolar and bipolar electrical stimulation of the motor cortex." *Acta Neurochirurgica* 141 (12):1295-301.

LaBarge, E., D. Edwards, and J. W. Knesevich. 1986. "Performance of normal elderly on the Boston Naming Test." *Brain Lang* 27 (2):380-4. doi: 10.1016/0093-934x(86)90026-x.

MacDonald, D. B., C. Dong, R. Quatrale, F. Sala, S. Skinner, F. Soto, and A. Szelenyi. 2019. "Recommendations of the International Society of Intraoperative Neurophysiology for intraoperative somatosensory evoked potentials." *Clin Neurophysiol* 130 (1):161-179. doi: 10.1016/j.clinph.2018.10.008.

Musizza, B., and S. Ribaric. 2010. "Monitoring the depth of anaesthesia." *Sensors* 10 (12):10896-935.

Nathan, S. S., S. R. Sinha, B. Gordon, R. P. Lesser, and N. V. Thakor. 1993. "Determination of current density distributions generated by electrical stimulation of the human cerebral cortex." *Electroencephalogr Clin Neurophysiol* 86 (3):183-92. doi: 10.1016/0013-4694(93)90006-h.

Neuloh, G., U. Pechstein, C. Cedzich, and J. Schramm. 2004. "Motor evoked potential monitoring with supratentorial surgery." *Neurosurgery* 54 (5):1061-70; discussion 1070-2. doi: 10.1227/01.neu.0000119326.15032.00.

Penfied, W., and T. Rasmussen. 1950. *The cerebral cortex of man; a clinical study of localization of function*: Macmillan.

Penfield, W., and E. Boldrey. 1937. "Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation." *Brain* 60 (4):389-443.

Raabe, A., J. Beck, P. Schucht, and K. Seidel. 2014. "Continuous dynamic mapping of the corticospinal tract during surgery of motor eloquent brain tumors: evaluation of a new method." *J Neurosurg* 120 (5):1015-24. doi: 10.3171/2014.1.JNS13909.

Rossi, M., M. Conti Nibali, L. Vigano, G. Puglisi, H. Howells, L. Gay, T. Sciortino, A. Leonetti, M. Riva, L. Fornia, G. Cerri, and L. Bello. 2019. "Resection of tumors within the primary motor cortex using high-frequency stimulation: oncological and functional efficiency of this

versatile approach based on clinical conditions." *J Neurosurg*:1-13. doi: 10.3171/2019.5.JNS19453.

Roth, J., A. Korn, F. Sala, H. Benvenisti, M. Jubran, Y. Bitan-Talmor, M. Ekstein, and S. Constantini. 2020. "Intraoperative neurophysiology in pediatric supratentorial surgery: experience with 57 cases." *Childs Nerv Syst* 36 (2):315-324. doi: 10.1007/s00381-019-04356-0.

Sala, F., and P. Lanteri. 2003. "Brain surgery in motor areas: the invaluable assistance of intraoperative neurophysiological monitoring." *J Neurosurg Sci* 47 (2):79-88.

Seidel, K., J. Beck, L. Stieglitz, P. Schucht, and A. Raabe. 2013. "The warning-sign hierarchy between quantitative subcortical motor mapping and continuous motor evoked potential monitoring during resection of supratentorial brain tumors." *J Neurosurg* 118 (2):287-96. doi: 10.3171/2012.10.JNS12895.

Seidel, K., P. Schucht, J. Beck, and A. Raabe. 2020. "Continuous Dynamic Mapping to Identify the Corticospinal Tract in Motor Eloquent Brain Tumors: An Update." *J Neurol Surg A Cent Eur Neurosurg* 81 (2):105-110. doi: 10.1055/s-0039-1698384.

Sinha, S. R., L. Sullivan, D. Sabau, D. San-Juan, K. E. Dombrowski, J. J. Halford, A. J. Hani, F. W. Drislane, and M. M. Stecker. 2016. "American Clinical Neurophysiology Society Guideline 1: Minimum Technical Requirements for Performing Clinical Electroencephalography." *J Clin Neurophysiol* 33 (4):303-7. doi: 10.1097/WNP.0000000000000308.

Szelényi, A., and L. Bello. 2010. "Intraoperative electrical stimulation in awake craniotomy: Methodological aspects of current practice." *Neurosurg Focus* 28:E7. doi: https://thejns.org/focus/view/journals/neurosurg-focus/28/2/article-pE7.xml.

Szelenyi, A., B. Joksimovic, and V. Seifert. 2007. "Intraoperative risk of seizures associated with transient direct cortical stimulation in patients with symptomatic epilepsy." *J Clin Neurophysiol* 24 (1):39-43. doi: 10.1097/01.wnp.0000237073.70314.f7.

Szelenyi, A., C. Senft, M. Jardan, M. T. Forster, K. Franz, V. Seifert, and H. Vatter. 2011. "Intra-operative subcortical electrical stimulation: a comparison of two methods." *Clin Neurophysiol* 122 (7):1470-5. doi: 10.1016/j.clinph.2010.12.055.

Talacchi, A., B. Santini, F. Casagrande, F. Alessandrini, G. Zoccatelli, and G. M. Squintani. 2013. "Awake surgery between art and science. Part I: clinical and operative settings." *Funct Neurol* 28 (3):205-21. doi: 10.11138/FNeur/2013.28.3.205.

Taniguchi, M., C. Cedzich, and J. Schramm. 1993. "Modification of cortical stimulation for motor evoked potentials under general anesthesia: technical description." *Neurosurgery* 32 (2):219-26.

Thirumala, P., D. Lai, J. Engh, M. Habeych, D. Crammond, and J. Balzer. 2013. "Predictive Value of Somatosensory Evoked Potential Monitoring during Resection of Intraparenchymal and Intraventricular Tumors Using an Endoscopic Port." *Journal of Clinical Neurology* 9 (4):244-51.

Yingling, C.D. 2011. "Intraoperative mapping and monitoring of motor cortex-A new paradigm." *US Neurol* 7 (1):64-67.

Zangaladze, A., A. Sharan, J. Evans, D. H. Wyeth, E. G. Wyeth, J. I. Tracy, I. Chervoneva, and M. R. Sperling. 2008. "The effectiveness of low-frequency stimulation for mapping cortical function." *Epilepsia* 49 (3):481-7. doi: 10.1111/j.1528-1167.2007.01307.x.

CHAPTER 5

SPINAL MAPPING: NEUROPHYSIOLOGISTS' PERSPECTIVE

PEDRO COELHO

Introduction

The spinal cord and its spinal nerves are of extreme functional importance. Monitoring such structures during surgery is crucial to secure favourable patient outcomes. The main objective of intra-operative neuromonitoring (IONM) is to prevent new neurological impairment by identifying it sufficiently early to allow prompt correction of its cause (Anonymous 1999). To optimally preserve neural structures during spinal surgery, an interdisciplinary effort between surgical, neurophysiology and anaesthetic personnel is imperative (Fagerlund and Eriksson 2009, Pajewski, Arlet, and Phillips 2007).

The recommended modalities for spine and spinal cord procedures are electro-encephalography (EEG), peripheral nerve stimulation with train-of-four (TOF), somatosensory evoked potentials (SSEPs), spontaneous and evoked (triggered) electromyography (EMG), and transcranial motor evoked potentials (TcMEP). In this chapter, various modalities and their interpretation are discussed; to rapidly understand which combinations of these are suited to which procedures, a lettering system is used.

Intra-operative neuromonitoring modalities

EEG (A)

EEG is the method of recording the spontaneous electrical activity of the brain. This varies enormously depending on the state of wakefulness of a patient. Adequate total intravenous anaesthesia (TIVA) with propofol and opioids results in a generalised slowing of the brain wave patterns (Figure 5-1). Higher doses of propofol can induce periods of low-voltage, almost isoelectric, activity alternating with high-voltage bursts of slow, sharp and spiking components – a pattern known as burst-suppression (Figure 5-2). As anaesthesia deepens, activity further reduces, giving way to longer periods of suppression, and finally electrocerebral silence (Figure 5-3). Sufficient EEG experience is required to interpret raw EEG signals and communicate these changes to the rest of the team.

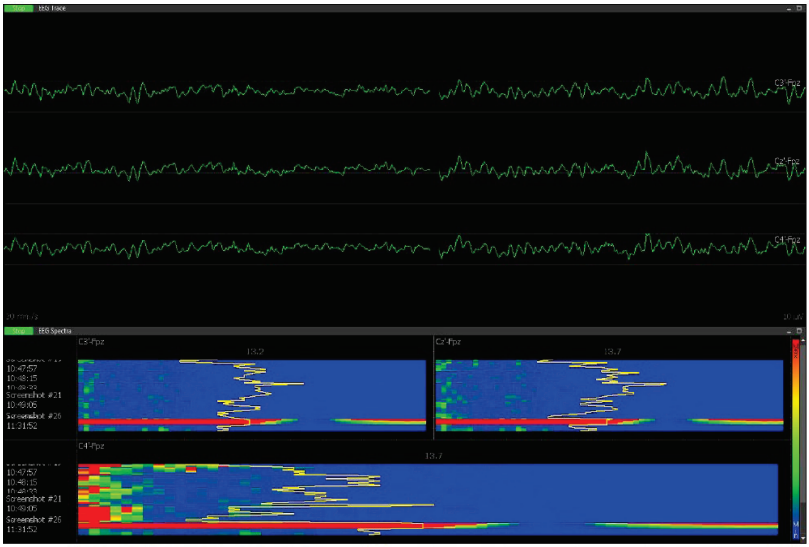

Fig. 5-1. Continuous EEG.

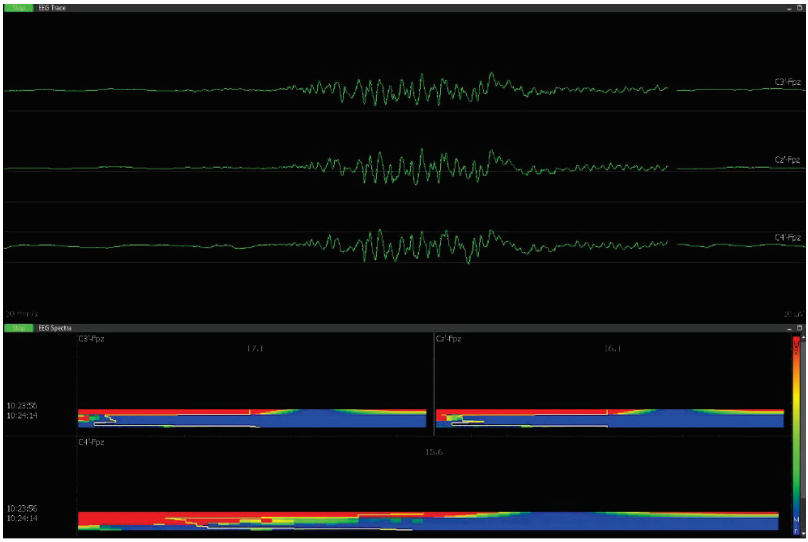

Fig. 5-2. Burst-suppression pattern on EEG.

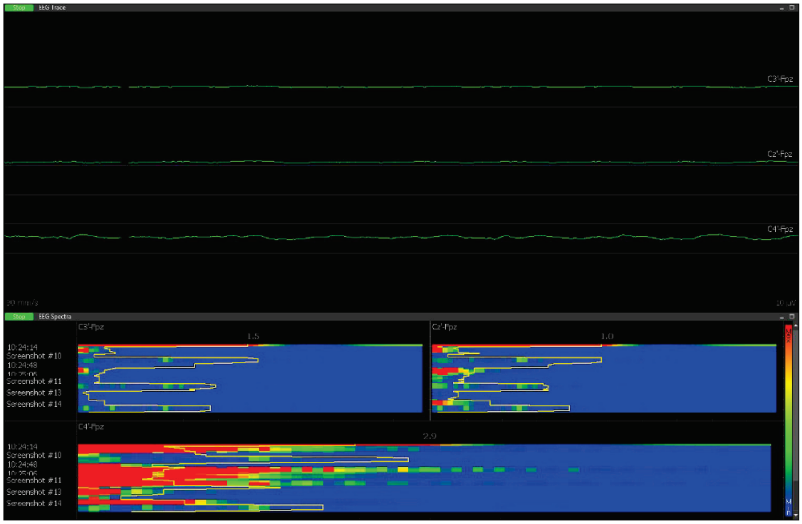

Fig. 5-3. Electrocerebral silence.

TOF (train-of-four) – peripheral monitoring of neuromuscular blockade (B)

Neuromuscular blocking agents (NMBAs) are routinely used during the induction of anaesthesia to facilitate tracheal intubation; they may also be administered to improve surgical conditions, such as in thoracolumbar spinal corrective surgery. NMBAs block transmission across the neuromuscular junction by interfering with the action of acetylcholine, which is released from the presynaptic terminal as a result of the depolarisation of a peripheral nerve (Fagerlund and Eriksson 2009). As these agents interfere with the recording of MEPs and EMG and can therefore mimic loss of neural function, short-acting NMBAs with a rapid offset are often preferred in neurosurgery. Their residual effect may be demonstrated by the use of a peripheral nerve stimulator capable of stimulation in a particular pattern, most commonly the train-of-four (TOF). This involves the delivery of four rapidly successive stimulating currents to a peripheral nerve (usually median, ulnar or posterior tibial); the number and amplitude of resultant muscle twitches correlate with the depth of neuromuscular blockade (Figure 5-4).

Fig. 5-4. Evolution of neuromuscular blockade with time. In this instance, 71 minutes had elapsed by the time the TOF recovered to 86% of baseline.

S-EMG (C) with T-EMG (D)

Intra-operative EMG is derived from needle electrodes placed directly into target muscles according to the structures at risk. Spontaneous EMG activity can be used to monitor the corresponding nerve roots responsible for muscle innervation. This technique does not require any directly-applied current because surgical manoeuvres such as compression, stretching, or dissection are usually followed by abnormal EMG discharges from the corresponding muscle groups.

EMG spikes and bursts can also be detected when incidental contact with neural tissue occurs. However, only "trains" of sustained firing are considered clinically significant – and should be reported to the surgeon immediately (Figure 5-5).

A Train – Sudden, rhythmic, uniform discharge, high frequency ≥150 Hz, variable amplitude

B Train – Irregular, semi-rhythmic spikes, different frequencies, crescendo-decrescendo pattern

C Train – Continuous activity of different overlapping components with different amplitudes, polyrhythmic

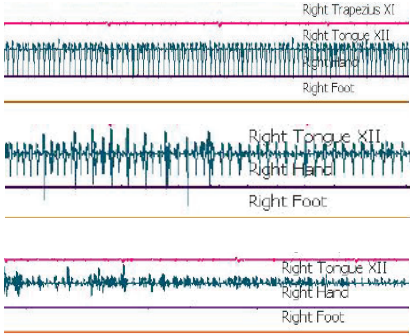

Fig. 5-5. Spontaneous EMG recording demonstrating different trains of activity in the muscles of the tongue.

Spontaneous trains of activity represent continuous, repetitive EMG firing caused by constant pressure applied to a given nerve root. Higher frequency bursts and/or amplitude tend to represent significant nerve fibre recruitment caused by excessive force, and indicate likely nerve injury (Romstock, Strauss, and Fahlbusch 2000).

The EMG is altered in patients with muscular dystrophies, inflammatory myopathies or disorders of the neuromuscular junction. In these conditions, baseline values may be of greater importance for later comparison. More frequently, EMG acquisition may be limited by excessive adipose tissue as

it increases the physical distance between active muscle fibres and related detection sites (Kuiken, Lowery, and Stoykov 2003). The modality is also sensitive to exogenous interference from electrosurgical equipment, high-speed drills and friction of surgical instruments.

Triggered, or evoked, EMG is used to identify a nerve root or a nerve, to access the functional integrity of such a structure, or to assess the correct placement of pedicle screws. Healthy neural tissue responds to a stimulus under 2 mA and produces a recordable compound muscle action potential (CMAP). The stimulus thresholds of chronically compressed nerve roots significantly outstrip those of normal roots and indicate partial axonal loss (axonotmesis). In such cases, the direct stimulus thresholds frequently exceed 10 mA (Holland et al. 1998).

SSEPs (E)

This modality is used to assess intra-operative neural function during a wide variety of spinal procedures. It provides monitoring of the dorsal column-medial lemniscus pathway, which is responsible for vibration sensation, tactile discrimination, form recognition, and joint/muscle sensation (conscious proprioception) (Kritchevsky and Wiederholt 1978) (Chiappa and Hill 1997). Several receptors in the skin, tendons, and muscles generate signals that correspond to these primary sensory modalities; these are then transmitted to neurones whose soma are located in dorsal root ganglia at all spinal cord levels. Axons from these first-order neurones project to the spinal cord via the medial root entry zone, giving rise to the fasciculus gracilis and cuneatus. These fasciculi carry sensory information from the lower and upper extremities, respectively, to the somatosensory cortex. The first synapse occurs in the lower medulla after these tracts ascend via the dorsal columns in the spinal cord. Following decussation at the medulla, the medial lemniscus is formed; it ascends to the thalamus and ultimately provides sensory information to the primary somatosensory cortex (Brodmann areas 3, 1, and 2).

Given that SSEPs monitor essentially the dorsal column–medial lemniscus pathway, appropriate sensory examination for fine touch (tactile discrimination), vibration sensation, and joint/muscle sensation (conscious proprioception) should be performed before surgery, to document any deficits that may limit intra-operative monitoring (Gonzalez et al. 2009). Standard electrode placement may be seen in Figures 5-6 (upper limb) and 5-8 (lower limb). Examples of normal SSEP recordings can be seen in Figures 5-7 (upper limb) and 5-9 (lower limb).

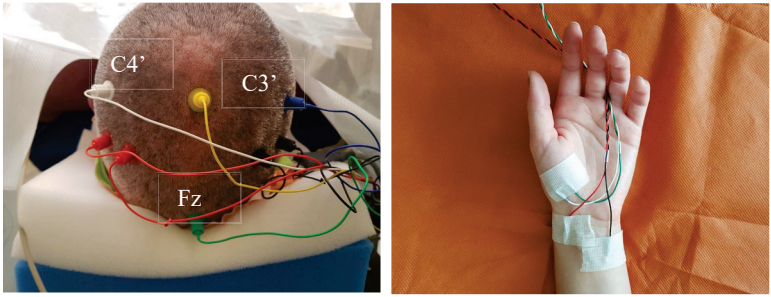

Fig. 5-6. SSEP electrode placement for the upper limb (median nerve). C4'-Fz denotes the left upper limb, and C3'-Fz, the right (the patient is positioned prone). Typical values for the upper limb would be 15 mA stimulations at a frequency of 3.7 Hz.

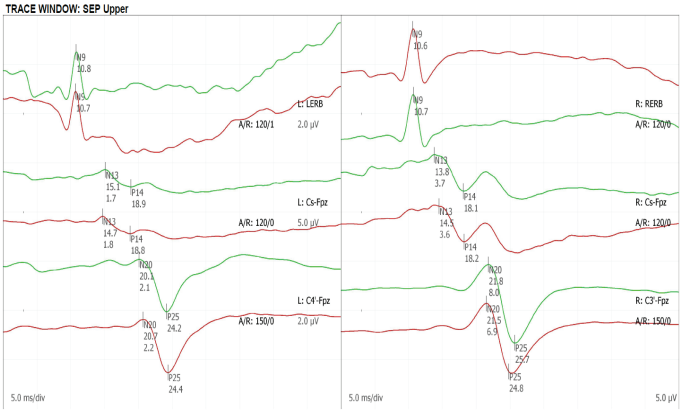

Fig. 5-7. Normal and stable upper limb SSEPs, including cortical, subcortical and peripheral waveforms.

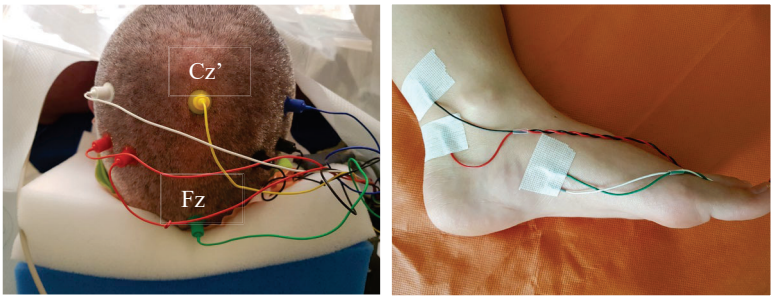

Fig. 5-8. SSEP electrode placement for the lower limb (posterior tibial nerve). Cz'-Fz indicates bilateral lower limb stimulation. Typical values for the lower limb would be 30 mA stimulations at a frequency of 2.7 Hz.

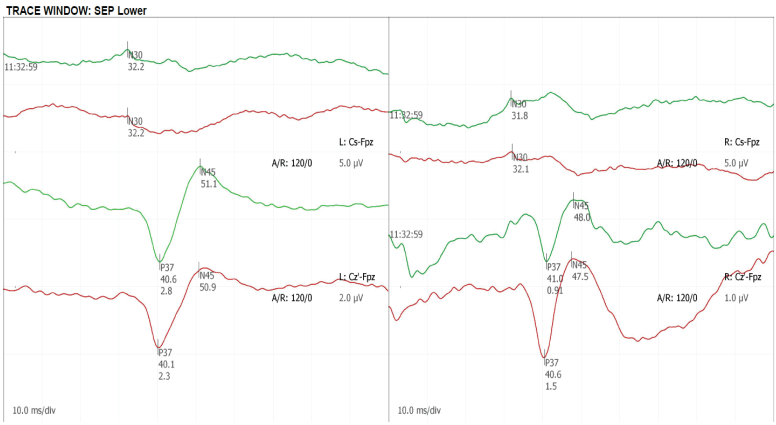

Fig. 5-9. Normal and stable lower limb SSEPs, including cortical and subcortical waveforms.

An experienced physiologist uses both latency and amplitude criteria for raising an alert. A 50% drop in amplitude of recorded potentials is conventionally—but arbitrarily—considered cause for concern (Nuwer et al. 1995). Amplitude may also be altered by halogenated anaesthetic agents, nitrous oxide, hypothermia, hypotension, and electrical interference. A reduction in latency of more than 5–10% may also trigger an alert, although this parameter is also affected by physiological conditions such as temperature. Both amplitude and latency tend to be affected for the first 20-30 minutes after induction of general anaesthesia as the nervous system equilibrates.

MEPs (F)

Corticospinal tracts are not monitored by SSEPs, as demonstrated by several reports of motor deficits following surgery in which SSEPs alone were used (Nuwer et al. 1995) (Lesser et al. 1986) (Ben-David, Haller, and Taylor 1987) (Chatrian, Berger, and Wirch 1988) (Tan et al. 2007). Before to the widespread use of MEP monitoring, the only definitive way to assess corticospinal tract integrity during surgery was the "Stagnara" wake-up test, which involved reducing anaesthesia and waking patients intra-operatively, and asking them to move their lower limbs (Ben-David, Taylor, and Haller 1987) (Vauzelle, Stagnara, and Jouvinroux 1973). Changes in MEPs now allow prediction of postoperative motor deficits whilst under anaesthesia (Bose, Sestokas, and Schwartz 2004) (Hilibrand et al. 2004) (Hsu et al. 2008).

The corticospinal tract and dorsal columns have different vascular supplies, with the latter receiving generous perfusion via the paired posterior spinal arteries. The lateral and anterior corticospinal tracts and the anterior horn cells receive the majority of their blood supply from the singular anterior spinal artery. Corrective manoeuvres during scoliosis surgery can cause compression of small radiculo-medullary arteries, resulting in subsequent ischemia or infarction. This can lead to postoperative motor deficits.

MEPs are usually stimulated either transcranially with spiral corkscrew electrodes, or via direct cortical stimulation with a strip electrode or monopolar probe. These evoked potentials may elicit signal recordings at the level of the muscle (CMAP), nerve, or spinal cord (direct corticospinal wave [D-wave] recording) (Aglio et al. 2002).

Scalp stimulating arrays are placed at measured sites over the motor cortex (Figure 5-10). For traditional transcranial MEP recording (TcMEP), stimulation electrodes are placed at C3 and C4, which evoke both upper and lower extremity MEPs. Alternative sites at C1 and C2 may be used if more focal activation of the lower extremity muscle groups is required (Sala, Krzan, and Deletis 2002) (Macdonald 2006) (Macdonald, Al Zayed, and Al Saddigi 2007) (Szelenyi, Kothbauer, and Deletis 2007). TcMEPs often produce bilateral responses, with a lower threshold and higher amplitude contralateral to the anode (ipsilateral with non-decussation). Anode switching allows symmetrical assessment, for example, C1–C2 followed by C2–C1 for right and then left MEPs (reversed for non-decussation). Using biphasic pulses may produce symmetrical MEPs, but cannot assess decussation, and might generate stronger patient movements. The C1/C2

level is a less potent stimulus than C3/C4, probably because more current shunts through the scalp (Holdefer, Sadleir, and Russell 2006); it therefore produces less patient movement. Stimulation of C3/C4 may be used in selected patients but causes stronger movement and may promote deeper current penetration. Switching to C3/4 during surgery may occasionally be required to restore fading C1/2 MEPs (Macdonald, Al Zayed, and Al Saddigi 2007). Table 1 summarises the common nerve root-muscle myotomal distributions.

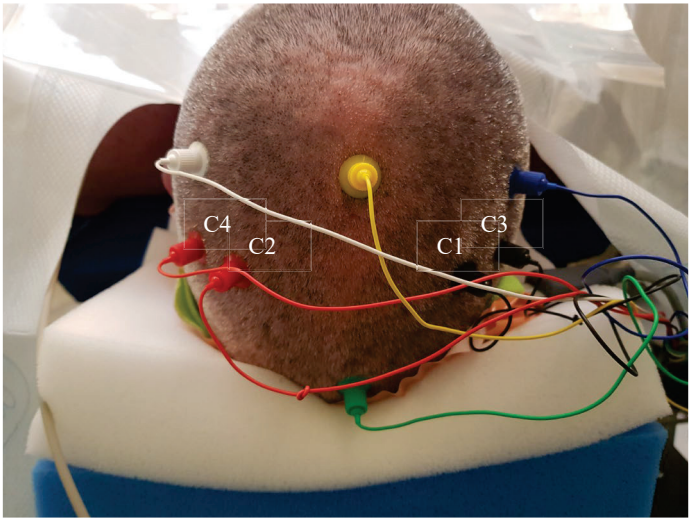

Fig. 5-10. Transcranial electric stimulation array in situ with the patient in the prone position.

Table 1. Common nerve root-muscle myotomal distributions.

ROOT	*NERVE*	*MUSCLE*
C3, C4	accessory	trapezius
C5, C6	axillary	deltoid
C5, C6	musculocutaneous	biceps brachii
C6, C7	radial	triceps
C8, **T1**	median	abductor pollicis brevis
C8, T1	ulnar	abductor digiti minimi
C8, T1	ulnar	adductor pollicis

C8, T1	ulnar	first dorsal interosseus
T7-T12		external oblique
T7-T12		rectus abdominis
L2, **L3**, L4	lumbar plexus	iliacus
L2, **L3**, **L4**	femoral	vastus lateralis/medialis
L2, **L3**, **L4**	femoral	rectus femoris
L4, **L5**, S1	sciatic	semitendinosus/membranosus
L4, **L5**	peroneal	tibialis anterior
L5, S1	peroneal	extensor hallucis
L5, S1	peroneal	extensor digitorum brevis
L5, **S1**	tibial	gastrocnemius lateral
S1, S2	tibial	gastrocnemius medial
S1, **S2**	tibial	abductor hallucis
S3, **S4**, **S5**	pudendal	external anal sphincter
S3, **S4**, **S5**	pudendal	external urethral sphincter

Interpretation of MEP recordings

Variability, anaesthetic factors, fade, and high sensitivity make muscle MEP interpretation prone to difficulty and controversy (Macdonald 2006).

Currently, four methods are routinely used for interpretation of TcMEP responses:

a) the presence or disappearance criterion
b) the amplitude reduction criterion
c) the threshold elevation criterion
d) the morphology simplification criterion.

The presence or disappearance criterion is the most widely-used method, given the inherent variability of signals in MEP monitoring (Kothbauer, Deletis, and Epstein 1998). A complete loss of the MEP signal is the visual disappearance of a response at the same display sensitivity that had previously contained consistent MEPs and is always a major alert criterion; as irreversible disappearance is a strong predictor of new motor weakness (although not necessarily severe or permanent) (Macdonald, Al Zayed, and

Al Saddigi 2007) (Kothbauer, Deletis, and Epstein 1998) (Quinones-Hinojosa et al. 2005) (Sala et al. 2006).

The amplitude reduction criterion uses an 80% amplitude decrement in at least one of six recording sites as an indicator of significant change (Langeloo et al. 2003).

The threshold elevation criterion is based on the stimulation threshold reaching or exceeding a predefined limit above baseline. The best-developed example comprises a 100 V or greater elevation, using 3–4 C3/4 constant-voltage 0.05 ms pulses with 2 ms intervals; this is based on anaesthesia with propofol, opioid and nitrous oxide, without NMBA (Calancie et al. 1998) (Calancie et al. 2001). An increment in voltage correlates with mild weakness, while concurrent or delayed disappearance is associated with greater weakness.

Finally, the morphology simplification criterion predicts impaired motor conduction of the corticospinal tracts by tracking changes in MEP waveform morphology. The basis for this is that pathological loss of motor units could reduce polyphasia without affecting overall amplitude (Quinones-Hinojosa et al. 2005). This study showed that changes persisted even after raising the threshold voltage by an average of 175 V, and that this correlated significantly with postoperative motor deficits.

Limitations of MEPs

MEPs have become the gold standard for monitoring of the motor tracts intra-operatively. However, there are still some limitations. TcMEPs recorded from the target muscles are generally followed by movement, meaning that the surgical procedure needs to be briefly interrupted. Continuous monitoring can therefore only be accomplished with SSEPs, with MEPs being obtained intermittently. Another limitation is that MEPs are currently contraindicated in patients with deep brain stimulators or cochlear implants.

Despite being a generally safe technique, tongue laceration can occur due to forced contraction of facial muscles (Macdonald 2006). Therefore, a bite block is routinely placed between the molars and front teeth to reduce such complications.

D-waves (G)

Electrically-stimulated motor cortex generates several synchronised descending volleys in the pyramidal tract. This knowledge is the foundation for the methodology of recording MEPs directly from the spinal cord (D-waves [direct] and I-waves [indirect]). This technique requires the placement of a recording electrode within the epidural space and has limitations to record signals below the level of T11. The utility of this modality has been reported during intramedullary spinal cord tumour resection (Deletis and Sala 2008) (Sala 2009). The neurophysiological principles for eliciting MEPs following the stimulation of the motor cortex in patients under general anaesthesia (GA) are different to those applied in awake patients. The absence of synapses between the stimulated cortical pyramidal neurones and the MEP recording site (spinal cord) allows single-pulse stimulation to activate axons of the cortical motor neurones, directly generating D-waves. The lack of synapses also makes D-waves relatively insensitive to anaesthesia. D-waves tend to be highly consistent but are generally small enough to require averaging of a number of responses. The amplitude correlates with the number of rapidly-conducting corticospinal tract axons within the spinal cord at the level of interest. D-waves are of higher amplitude in the upper than lower regions of the cord; monitoring is not usually practical below the level of T10, due to the small number of corticospinal tract fibres that remain (Legatt et al. 2016). Normal D-wave recordings may be seen in Figure 5-11.

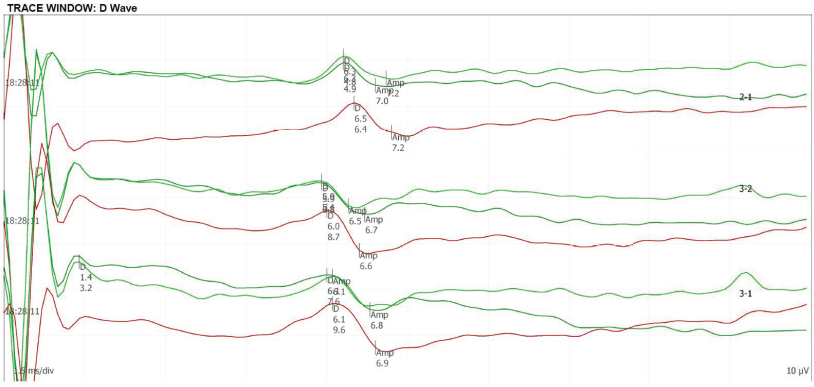

Fig. 5-11. Normal D-wave recordings.

D-waves have been shown to be closely correlated with postoperative clinical status; a complete loss of muscle MEPs with at least 50% preservation of the D-wave amplitude generally results in transient paraplegia only. Conversely, patients with complete loss of the D-wave during surgery are likely to have permanent motor deficits (Morota et al. 1997).

The D-wave amplitude is greatest when the bipolar recording electrode is near the spinal cord, which is the rationale for invasive recording. A 2–3 cm inter-electrode distance is optimal; a shorter distance reduces amplitude, and longer introduces noise. For fixed spinal cord electrode and inter-electrode distances, D-wave amplitude is proportional to the number of synchronously conducting corticospinal axons at the recorded level (Gonzalez et al. 2009) (Deletis 1993) (Amassian 2002).

Intra-operative neuromonitoring of spinal procedures

MEP monitoring is currently used in a variety of spinal operations, including the correction of spinal deformity, cervical and thoracolumbar degenerative cases, and resection of spinal cord tumours.

Cervical spine

Cervical spine surgery is generally performed for treatment of radiculopathy, spinal cord compression or spinal instability causing weakness and pain. Anterior cervical decompression and fusion (ACDF), cervical corpectomy, posterior cervical fusion, and ossification of the posterior longitudinal ligament are a few examples of procedures in which IONM is commonly used.

Modalities **A, B, C, E, and F** are recommended.

Thoracic spine

The thoracic spine connects the cervical and lumbar portions of the spine and consists of twelve vertebrae (T1 to T12). The thoracic spine provides sufficient stability to keep the body in the upright position. The intent of surgery in this area is generally to improve the quality of life.

Scoliosis correction

Scoliosis describes an abnormal sideways curvature of the spine. Over the past two decades, instrumentation and fusion using pedicle screws have become the standard for spinal stabilisation. A risk of pedicle screw placement is medial screw breach through the pedicle wall and into the spinal canal, posing a threat to the exiting nerve root at that level. Triggered EMG can determine whether this has occurred (Gonzalez et al. 2009). A threshold inferior to 10 mA for pedicle screw stimulation, or 7 mA for monopolar probe stimulation inside the pedicle wall, suggests a medial wall breach in the lumbar pedicles (Calancie, Madsen, and Lebwohl 1994). A triggered EMG threshold response between 10 and 20 mA suggests a low probability of breach of the medial wall, whereas thresholds above 15 mA indicate a 98% likelihood of accurate screw positioning on postoperative CT scan (Shi et al. 2003). Thresholds above 20 mA are most reassuring that there is no breach of the pedicle wall. At the thoracic level, pedicle screw placement with stimulation thresholds under 6 mA suggest a medial pedicle breach (Raynor et al. 2002).

Modalities **A, B, C, D, E and F** are recommended.

Lumbosacral spine

The lumbar spine supports the weight of the body. Common surgically amenable conditions that cause lower back and lower extremity pain include disc herniation, degenerative disc disease, spondylolisthesis, spinal stenosis and sacro-iliac joint dysfunction. Posterior lumbar interbody fusion, anterior lumbar interbody fusion and extreme lateral interbody fusion are examples of procedures where IONM is used.

Modalities **A, B, C, D, E and F** are recommended.

Intra-operative neuromonitoring of spinal cord procedures

Intramedullary tumours

The surgical treatment of spinal cord tumours can be challenging because such pathology and its management are associated with an increased risk of neurological deficits compared with more routine spinal procedures (Raynor et al. 2002) (Hoshimaru et al. 1999).

Spinal cord tumours can be classified as extradural, intradural/extramedullary and intradural/intramedullary. Extradural tumours are within the spine but outside the sac (dura). This thick membrane contains the spinal cord, nerve roots and cerebrospinal fluid. Intradural tumours are within the dural sac and can either be extramedullary (outside the spinal cord) or intramedullary (within the spinal cord). The aim of IONM in these cases is to maximise tumour resection while preserving neurological function to the greatest extent possible.

Such procedures require comprehensive IONM: modalities **A, B, C, D, E, and F** are applicable. Upper extremity SSEPs are particularly relevant in the removal of cervical lesions and to monitor for positioning-related neuropathy (e.g. peripheral nerves and/or brachial plexus) during procedures of the thoracolumbar cord. Lower extremity SSEPs are important in the resection of thoracic and lumbosacral lesions.

Intramedullary spinal cord tumours often alter the cord anatomy. Discrimination of viable dorsal columns versus inert tissue is crucial for determining safe incision sites and avoiding postoperative neurological deficits (Nair et al. 2014). This can be achieved by dorsal column mapping via a method known as phase reversal. The right and left dorsal columns are stimulated, and the triggered SSEPs recorded from the scalp. Phase reversal and amplitude changes are then reported to the surgeon, who will be able to identify dorsal column laterality and the inert median raphe, as well as other safe incision sites (Nair et al. 2014). However, SSEPs may be lost following myelotomy (Whittle, Johnston, and Besser 1986). MEPs become important during manipulation of the cleavage plane between the tumour and spinal cord. Unlike SSEPs, which may be continuously run, MEPs cause patient movement and require a pause in surgery before stimulation (Whittle, Johnston, and Besser 1986).

In order to continuously monitor MEPs, the use of D-waves is paramount. By placing an epidural spinal electrode medially over the spinal cord, it is possible to record the D-wave resulting from a single transcranial pulse as it travels along the corticospinal tract in the spinal cord (Katayama et al. 1988). This single transcranial pulse, while sufficient to elicit a D-wave, is not enough to cause depolarisation and firing of the lower motor neurones (which would cause movement). This makes the D-wave modality ideal for continuous monitoring of corticospinal tract function during resection of intramedullary spinal cord tumours. It is also highly specific for the corticospinal tract, unlike muscle MEPs, which depend on the function of additional descending tracts (Sala et al. 2007).

Spinal cord untethering

Surgery to the cauda equina carries the risk of serious complications, including paralysis. Tethered cord occurs when there is an abnormal attachment of the spinal cord to other tissues, limiting its movement within the thecal sac (Woods et al. 2010). There are numerous causes of tethered cord, with the predominant one being a type of neural tube defect known as spinal dysraphism (Paradiso et al. 2005). This defect may be open or closed (occult). Open dysraphisms comprise myelomeningocele, where the spinal cord and meninges protrude from the back, and meningocele, where only the meninges are protruding. As these are visually obvious, they are diagnosed prenatally or shortly after birth. Lipomyelomeningocele is a common type of occult spinal dysraphism. It is characterised by a lipoma that attaches to the spinal cord and is covered by skin. The several attachments of the spinal cord exhibited in these conditions prevent the cord from ascending to the usual T12-L1 vertebral level in adults. This causes metabolic changes in the spinal cord (conus medullaris) as a result of spinal cord stretch and resultant vascular insufficiency (Kang et al. 1987). The cauda equina itself is also stretched, including the sacral nerve roots that mediate bowel and bladder function, resulting in corresponding symptoms.

Monitoring for spinal cord untethering

The several nerve roots that constitute the cauda equina are the structures at the greatest risk. Once these neural elements are reached, the nerve roots are identified and released from their attachments. The filum terminale is also identified following direct nerve stimulation, and if found to be contributing to the tethering, is cut. Spontaneous EMG is an important modality used to monitor the activity of nerve roots during the procedure (Paradiso et al. 2006); stimulation of the nerve roots can help identify their level of origin and whether or not they are healthy (Quinones-Hinojosa et al. 2004). Triggered EMG is used to help the surgeon identify functional nerve roots (Paradiso et al. 2005) (Quinones-Hinojosa et al. 2004). Often it is impossible to visually identify nerve roots in the presence of tissue adhesions or a lipoma, and so the surgeon must rely on electrical stimulation to discriminate between neural and inert tissue (Legatt et al. 1992).

MEPs are also monitored during spinal cord untethering (Nagle et al. 1996). This modality is highly sensitive to ischaemia – a particular risk in these procedures – and highly specific for nerve root injury. A loss of response from a muscle may be an indicator of injury to the nerve roots innervating that particular muscle. Like other procedures utilising MEPs, recordings

should be obtained as often as is practical during surgery, especially the time from untethering through to closure of the skin.

Modalities **A, B, C, D, E and F** are recommended.

References

Aglio, L. S., R. Romero, S. Desai, M. Ramirez, A. A. Gonzalez, and L. D. Gugino. 2002. "The use of transcranial magnetic stimulation for monitoring descending spinal cord motor function." *Clinical Electroencephalography* 33 (1):30-41.

Amassian, V.E. 2002. "Animal and human motor system neurophysiology related to intraoperative monitoring." In *Neurophysiology in neurosurgery*, edited by V. Deletis and Shils JL, 3-23. San Diego: Academic Press.

Anonymous. 1999. "Recommendations for the practice of clinical neurophysiology: guidelines of the International Federation of Clinical Neurophysiology." *Electroencephalography & Clinical Neurophysiology - Supplement* 52:1-304.

Ben-David, B., G. Haller, and P. Taylor. 1987. "Anterior spinal fusion complicated by paraplegia. A case report of a false-negative somatosensory-evoked potential." *Spine* 12 (6):536-9.

Ben-David, B., P. D. Taylor, and G. S. Haller. 1987. "Posterior spinal fusion complicated by posterior column injury. A case report of a false-negative wake-up test." *Spine* 12 (6):540-3.

Bose, B., A. K. Sestokas, and D. M. Schwartz. 2004. "Neurophysiological monitoring of spinal cord function during instrumented anterior cervical fusion." *Spine Journal: Official Journal of the North American Spine Society* 4 (2):202-7.

Calancie, B., W. Harris, G. F. Brindle, B. A. Green, and H. J. Landy. 2001. "Threshold-level repetitive transcranial electrical stimulation for intraoperative monitoring of central motor conduction." *Journal of Neurosurgery* 95 (2 Suppl):161-8.

Calancie, B., W. Harris, J. G. Broton, N. Alexeeva, and B. A. Green. 1998. ""Threshold-level" multipulse transcranial electrical stimulation of motor cortex for intraoperative monitoring of spinal motor tracts: description of method and comparison to somatosensory evoked potential monitoring." *Journal of Neurosurgery* 88 (3):457-70.

Calancie, B., P. Madsen, and N. Lebwohl. 1994. "Stimulus-evoked EMG monitoring during transpedicular lumbosacral spine instrumentation. Initial clinical results." *Spine* 19 (24):2780-6.

Chatrian, G. E., M. S. Berger, and A. L. Wirch. 1988. "Discrepancy between intraoperative SSEP's and postoperative function. Case report." *Journal of Neurosurgery* 69 (3):450-4.

Chiappa, K., and R. Hill. 1997. "Short Latency Somatosensory Evoked Potentials: methodology." In *Evoked Potentials in Clinical Medicine* edited by Chiappa K, 283-340. Philadelphia: Lippincott-Raven.

Deletis, V. 1993. "Intraoperative Monitoring of the Functional Integrity of the Motor Pathways." In *Electrical and magnetic stimulation of the brain and spinal cord*, edited by O. Devinsky, A. Beric and M. Dogali, 201-214. New York: Raven Press Ltd.

Deletis, V., and F. Sala. 2008. "Intraoperative neurophysiological monitoring of the spinal cord during spinal cord and spine surgery: a review focus on the corticospinal tracts." *Clinical Neurophysiology* 119 (2):248-64.

Fagerlund, M. J., and L. I. Eriksson. 2009. "Current concepts in neuromuscular transmission." *British Journal of Anaesthesia* 103 (1):108-14.

Gonzalez, A. A., D. Jeyanandarajan, C. Hansen, G. Zada, and P. C. Hsieh. 2009. "Intraoperative neurophysiological monitoring during spine surgery: a review." *Neurosurgical Focus* 27 (4):E6.

Hilibrand, A. S., D. M. Schwartz, V. Sethuraman, A. R. Vaccaro, and T. J. Albert. 2004. "Comparison of transcranial electric motor and somatosensory evoked potential monitoring during cervical spine surgery." *Journal of Bone & Joint Surgery - American Volume* 86 (6):1248-53.

Holdefer, R. N., R. Sadleir, and M. J. Russell. 2006. "Predicted current densities in the brain during transcranial electrical stimulation." *Clinical Neurophysiology* 117 (6):1388-97.

Holland, N. R., T. A. Lukaczyk, L. H. Riley, 3rd, and J. P. Kostuik. 1998. "Higher electrical stimulus intensities are required to activate chronically compressed nerve roots. Implications for intraoperative electromyographic pedicle screw testing." *Spine* 23 (2):224-7.

Hoshimaru, M., T. Koyama, N. Hashimoto, and H. Kikuchi. 1999. "Results of microsurgical treatment for intramedullary spinal cord ependymomas: analysis of 36 cases." *Neurosurgery* 44 (2):264-9.

Hsu, B., A. K. Cree, J. Lagopoulos, and J. L. Cummine. 2008. "Transcranial motor-evoked potentials combined with response recording through compound muscle action potential as the sole modality of spinal cord monitoring in spinal deformity surgery." *Spine* 33 (10):1100-6.

Kang, J. K., M. C. Kim, D. S. Kim, and J. U. Song. 1987. "Effects of tethering on regional spinal cord blood flow and sensory-evoked potentials in growing cats." *Childs Nervous System* 3 (1):35-9.

Katayama, Y., T. Tsubokawa, S. Maejima, T. Hirayama, and T. Yamamoto. 1988. "Corticospinal direct response in humans: identification of the motor cortex during intracranial surgery under general anaesthesia." *Journal of Neurology, Neurosurgery & Psychiatry* 51 (1):50-9.

Kothbauer, K. F., V. Deletis, and F. J. Epstein. 1998. "Motor-evoked potential monitoring for intramedullary spinal cord tumor surgery: correlation of clinical and neurophysiological data in a series of 100 consecutive procedures." *Neurosurgical Focus* 4 (5):e1.

Kritchevsky, M., and W. C. Wiederholt. 1978. "Short-latency somatosensory evoked potentials." *Archives of Neurology* 35 (11):706-11.

Kuiken, T. A., M. M. Lowery, and N. S. Stoykov. 2003. "The effect of subcutaneous fat on myoelectric signal amplitude and cross-talk." *Prosthetics & Orthotics International* 27 (1):48-54.

Langeloo, D. D., A. Lelivelt, H. Louis Journee, R. Slappendel, and M. de Kleuver. 2003. "Transcranial electrical motor-evoked potential monitoring during surgery for spinal deformity: a study of 145 patients." *Spine* 28 (10):1043-50.

Legatt, A. D., R. G. Emerson, C. M. Epstein, D. B. MacDonald, V. Deletis, R. J. Bravo, and J. R. Lopez. 2016. "ACNS Guideline: Transcranial Electrical Stimulation Motor Evoked Potential Monitoring." *Journal of Clinical Neurophysiology* 33 (1):42-50.

Legatt, A. D., C. E. Schroeder, B. Gill, and J. T. Goodrich. 1992. "Electrical stimulation and multichannel EMG recording for identification of functional neural tissue during cauda equina surgery." *Childs Nervous System* 8 (4):185-9.

Lesser, R. P., P. Raudzens, H. Luders, M. R. Nuwer, W. D. Goldie, H. H. Morris, 3rd, D. S. Dinner, G. Klem, J. F. Hahn, A. G. Shetter, and et al. 1986. "Postoperative neurological deficits may occur despite unchanged intraoperative somatosensory evoked potentials." *Annals of Neurology* 19 (1):22-5.

Macdonald, D. B. 2006. "Intraoperative motor evoked potential monitoring: overview and update." *Journal of Clinical Monitoring & Computing* 20 (5):347-77.

Macdonald, D. B., Z. Al Zayed, and A. Al Saddigi. 2007. "Four-limb muscle motor evoked potential and optimized somatosensory evoked potential monitoring with decussation assessment: results in 206 thoracolumbar spine surgeries." *European Spine Journal* 16 Suppl 2:S171-87.

Morota, N., V. Deletis, S. Constantini, M. Kofler, H. Cohen, and F. J. Epstein. 1997. "The role of motor evoked potentials during surgery for intramedullary spinal cord tumors." *Neurosurgery* 41 (6):1327-36.

Nagle, K. J., R. G. Emerson, D. C. Adams, E. J. Heyer, D. P. Roye, F. J. Schwab, M. Weidenbaum, P. McCormick, J. Pile-Spellman, B. M. Stein, J. P. Farcy, E. J. Gallo, K. C. Dowling, and C. A. Turner. 1996. "Intraoperative monitoring of motor evoked potentials: a review of 116 cases." *Neurology* 47 (4):999-1004.

Nair, D., V. M. Kumaraswamy, D. Braver, R. D. Kilbride, L. F. Borges, and M. V. Simon. 2014. "Dorsal column mapping via phase reversal method: the refined technique and clinical applications." *Neurosurgery* 74 (4):437-46; discussion 446.

Nuwer, M. R., E. G. Dawson, L. G. Carlson, L. E. Kanim, and J. E. Sherman. 1995. "Somatosensory evoked potential spinal cord monitoring reduces neurologic deficits after scoliosis surgery: results of a large multicenter survey." *Electroencephalography & Clinical Neurophysiology* 96 (1):6-11.

Pajewski, T. N., V. Arlet, and L. H. Phillips. 2007. "Current approach on spinal cord monitoring: the point of view of the neurologist, the anesthesiologist and the spine surgeon." *European Spine Journal* 16 Suppl 2:S115-29.

Paradiso, G., G. Y. Lee, R. Sarjeant, and M. G. Fehlings. 2005. "Multi-modality neurophysiological monitoring during surgery for adult tethered cord syndrome." *Journal of Clinical Neuroscience* 12 (8):934-6.

Paradiso, G., G. Y. Lee, R. Sarjeant, L. Hoang, E. M. Massicotte, and M. G. Fehlings. 2006. "Multimodality intraoperative neurophysiologic monitoring findings during surgery for adult tethered cord syndrome: analysis of a series of 44 patients with long-term follow-up." *Spine* 31 (18):2095-102.

Quinones-Hinojosa, A., C. A. Gadkary, M. Gulati, C. S. von Koch, R. Lyon, P. R. Weinstein, and C. D. Yingling. 2004. "Neurophysiological monitoring for safe surgical tethered cord syndrome release in adults." *Surgical Neurology* 62 (2):127-33; discussion 133-5.

Quinones-Hinojosa, A., R. Lyon, G. Zada, K. R. Lamborn, N. Gupta, A. T. Parsa, M. W. McDermott, and P. R. Weinstein. 2005. "Changes in transcranial motor evoked potentials during intramedullary spinal cord tumor resection correlate with postoperative motor function." *Neurosurgery* 56 (5):982-93; discussion 982-93.

Raynor, B. L., L. G. Lenke, Y. Kim, D. S. Hanson, T. J. Wilson-Holden, K. H. Bridwell, and A. M. Padberg. 2002. "Can triggered electromyograph thresholds predict safe thoracic pedicle screw placement?" *Spine* 27 (18):2030-5.

Romstock, J., C. Strauss, and R. Fahlbusch. 2000. "Continuous electromyography monitoring of motor cranial nerves during cerebellopontine angle surgery." *Journal of Neurosurgery* 93 (4):586-93.

Sala, F. 2009. "Improving spinal cord monitoring: a neurosurgeon's view." *Clinical Neurophysiology* 120 (4):649-50.

Sala, F., A. Bricolo, F. Faccioli, P. Lanteri, and M. Gerosa. 2007. "Surgery for intramedullary spinal cord tumors: the role of intraoperative (neurophysiological) monitoring." *European Spine Journal* 16 Suppl 2:S130-9.

Sala, F., M. J. Krzan, and V. Deletis. 2002. "Intraoperative neurophysiological monitoring in pediatric neurosurgery: why, when, how?" *Childs Nervous System* 18 (6-7):264-87.

Sala, F., G. Palandri, E. Basso, P. Lanteri, V. Deletis, F. Faccioli, and A. Bricolo. 2006. "Motor evoked potential monitoring improves outcome after surgery for intramedullary spinal cord tumors: a historical control study." *Neurosurgery* 58 (6):1129-43; discussion 1129-43.

Shi, Y. B., M. Binette, W. H. Martin, J. M. Pearson, and R. A. Hart. 2003. "Electrical stimulation for intraoperative evaluation of thoracic pedicle screw placement." *Spine* 28 (6):595-601.

Szelenyi, A., K. F. Kothbauer, and V. Deletis. 2007. "Transcranial electric stimulation for intraoperative motor evoked potential monitoring: Stimulation parameters and electrode montages." *Clinical Neurophysiology* 118 (7):1586-95.

Tan, G., M. H. Craine, M. J. Bair, M. K. Garcia, J. Giordano, M. P. Jensen, S. M. McDonald, D. Patterson, R. A. Sherman, W. Williams, and J. C. Tsao. 2007. "Efficacy of selected complementary and alternative medicine interventions for chronic pain." *Journal of Rehabilitation Research & Development* 44 (2):195-222.

Vauzelle, C., P. Stagnara, and P. Jouvinroux. 1973. "Functional monitoring of spinal cord activity during spinal surgery." *Clinical Orthopaedics & Related Research* (93):173-8.

Whittle, I. R., I. H. Johnston, and M. Besser. 1986. "Recording of spinal somatosensory evoked potentials for intraoperative spinal cord monitoring." *Journal of Neurosurgery* 64 (4):601-12.

Woods, K. R., A. R. Colohan, S. Yamada, S. M. Yamada, and D. J. Won. 2010. "Intrathecal endoscopy to enhance the diagnosis of tethered cord syndrome." *Journal of Neurosurgery Spine* 13 (4):477-83.

CHAPTER 6

SPINAL SURGERY: SURGEONS' PERSPECTIVE

DANIEL OCHIENG

Introduction

The utility of intra-operative neuromonitoring (IONM) in operations involving the spinal cord has historically been fraught with controversy. Two schools of thought predominate: one surmises that IONM acts as an early warning system, lending the surgeon confidence to be more aggressive; while the opposing view holds that neuromonitoring may ultimately be detrimental, preventing the surgeon from achieving maximal resection. Whichever side one gravitates to, it is important that a surgeon gains a fundamental understanding of the principles of IONM and how to interpret its findings in relation to specific operations.

Grady Brooch once famously said, "A fool with a tool is still a fool". It is therefore important to remember that neuromonitoring is not a magic bullet to avoid all complications in spinal surgery. It should be viewed as an adjunct that needs the right indication, the right methodology and the right interpretation for it to be useful. The use of neuromonitoring should hence not be as simplistic as "always use it" or "never use it", but should be viewed in the context of the following questions: Is it useful in this case? Is it safe in this case? Will it unreasonably prolong the duration of surgery or increase the risk of complications?

Essential anatomy

The spinal cord is the distal extension of the medulla and extends from the region of the foramen magnum to the junction of the first and second lumbar vertebra. It is suspended within the vertebral canal, held in place by 21 pairs of denticulate ligaments, and attached distally to the S2 body via the filum

terminale. The spinal cord has 33 segments: eight cervical, twelve thoracic, five lumbar, five sacral and three coccygeal, with paired peripheral nerves arising on each side. Microscopically, the cord has an internal H-shaped grey matter core composed of neuronal cell bodies, and an outer white matter which consists of long (descending and ascending) and short (interconnecting) tracts of nerve fibres (Figure 6-1).

The spinal cord blood supply is predominantly from the anterior and posterior spinal arteries, which are in turn derived from the vertebral arteries (Figure 6-2). These are supplemented by segmental radicular arteries, of which the artery of Adamkiewicz is the largest. As a result, the spinal cord is sensitive to ischaemia and it is essential to ensure adequate perfusion during various operations of the vertebral column and spinal cord.

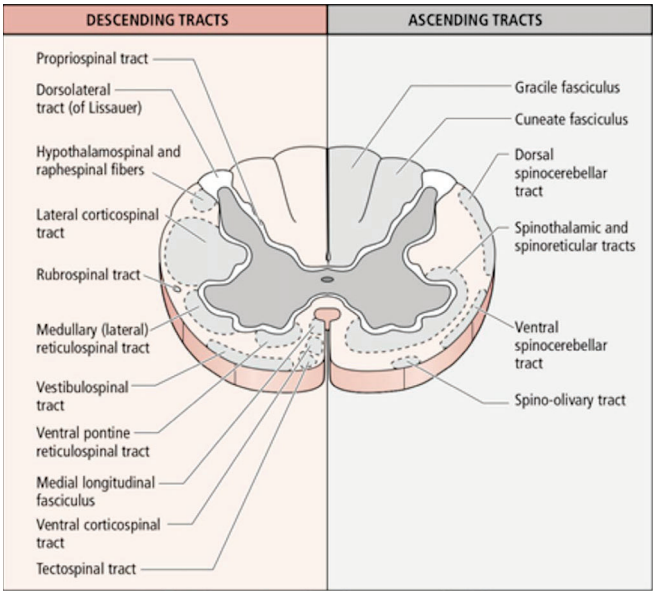

Fig. 6-1. Cross-sectional anatomy of the spinal cord. Note that while the ascending and descending tracts are depicted separately on either half of this diagram, both tracts are present bilaterally in life. Reproduced with permission (A Textbook of Neuroanatomy, Maria Patestas and Leslie Gartner. Blackwell Publishing 2006).

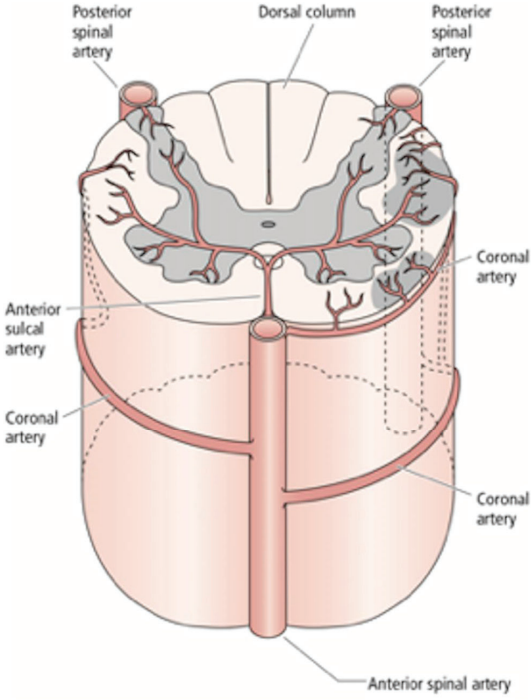

Fig. 6-2. Blood supply of the spinal cord. Reproduced with permission (A Textbook of Neuroanatomy, Maria Patestas and Leslie Gartner. Blackwell Publishing 2006).

Neurophysiologic principles

Neuromonitoring is based on the principle that complete conduction of electrophysiologic current requires intact or functioning connections between two points. This signal transmission is via saltatory conduction and occurs at a definite speed and voltage.

The quality of these signals, specifically the amplitude and latency, is closely monitored and any changes are interpreted in the context of surgical, anaesthetic and patient factors. Generally, an alarm is raised with a 50% reduction in amplitude and/or a 10% increase in latency in signals.

The following are the main modalities of IONM of use to the surgeon:

1. Motor Evoked Potentials (MEPs)
2. Somatosensory Evoked Potentials (SSEPs)
3. Direct waves (D-waves)
4. Multimodality neuromonitoring (often a combination of the above for control and redundancy)

MEPs are used to monitor the integrity of the corticospinal pathway. They are based on initial work by Merton and Morton (Merton and Morton 1980), who described transcranial magnetic stimulation of the motor cortex. They are sensitive to anaesthetics, especially volatile gases, which should be avoided. High frequencies of over 200 Hz and low voltages are often used. Responses to this stimulation are then recorded distally at the muscle or epidural electrodes placed distal to the region at risk (Figure 6-3).

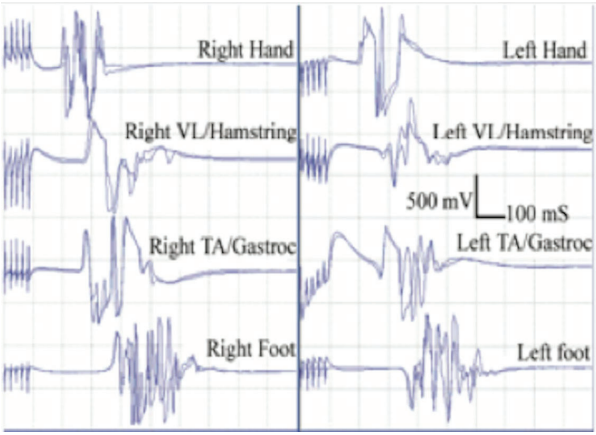

Fig. 6-3. MEPs recorded at the thenar muscles in the hand, vastus lateralis in the thigh, tibialis anterior in the leg, and abductor hallucis in the foot. Note the slight delay as the MEPs are recorded more distally. The values should be compared bilaterally.

SSEPs were initially described by Nash et al (Nash et al. 1977) and are recorded in a "retrograde" fashion, with the stimulating signal being applied to the limbs while the recording leads are often on the scalp. The nerves commonly used are the median and ulnar nerves for the upper limbs, and peroneal and posterior tibial nerves for the lower limbs (Figure 6-4). The posterior columns are the tracts predominantly monitored by this modality. The major criticisms for SSEPs are their low sensitivity for detection of nerve root injuries due to root traction or pedicle screw placement, and lag in change of SSEP signals when compared to MEPs (Hilibrand et al. 2004).

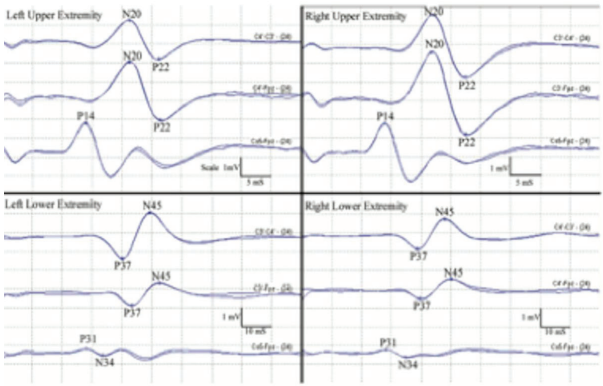

Fig. 6-4. SSEPs recorded bilaterally on the scalp after stimulation of the median nerve at the wrist.

D-waves are measured by electrodes placed in the epidural space caudal to the region at risk. The signals are generated via transcranial stimulation. The main advantage of this mode is the ability to use neuromuscular blockade during operations for both surgical and anaesthetic benefit. D-waves are also relatively resistant to anaesthetic influence. Their main limitation, however, is that they cannot monitor the distal cauda equina and nerve roots, as the recording electrode is over the spinal cord itself.

Multimodality neuromonitoring combines the advantages of several individual techniques while limiting risk. It provides a reference point for comparison, especially when troubleshooting for systemic issues that may cause false positives, such as the influence of anaesthetic agents. Its use necessarily lengthens the procedure time as multiple modes take longer to institute before the start of surgery.

In the use of neuromonitoring, the following four scenarios are possible (Rijs et al. 2019):

1. **True negative**: No IONM warning signs elicited during the procedure, and no deficit postoperatively. This is the ideal outcome.
2. **True positive**: IONM warning signs raised during the procedure, and correlating neurological deficit seen postoperatively (unless rectified intra-operatively). This is clinically undesirable but confirms reliability of the monitoring.

3. **False negative**: No IONM warning signs during the procedure, but neurologic deficit present postoperatively. This is the worst outcome and is to be avoided. It points to either poor selection of technique, failure of equipment, or false interpretation.
4. **False positive**: IONM warning signs present during the procedure, but no neurological deficit postoperatively. This may be interpreted in one of two ways:
   - Either the IONM warning signs were "true" markers of pending deficits that were then alleviated, preventing permanent deficit, *or*
   - The IONM warning signs were false and had led to premature abandonment of the procedure.

Pre-operative planning

Pre-operative discussions between the neurophysiology, anaesthetic and neurosurgical teams are vital to ensure the smooth utilisation of IONM. The type and goals of the neuromonitoring should be discussed.

The important questions to be considered are:

1. Who are the team members, and what are their roles?
2. What is the appropriate modality to be used?
3. What neurologic deficit is most likely to result from the procedure?
4. What anaesthetic protocol will optimise neuromonitoring signals?
5. Can neuromuscular blocking agents be used by the anaesthetist?
6. What alarm criteria should be used for each modality?
7. What steps should be taken in case of any concern?
8. Are any new techniques being implemented?

Tailoring of the monitoring technique to optimise outcome – but not unreasonably increase surgical time – is vital. For example, SSEPs alone may be adequate for posterior spinal decompression in laminectomies, where only the dorsal columns are at risk. This helps to avoid over-monitoring and reduces the risks associated with prolonged anaesthesia and procedural times.

It is also vital that an intra-operative checklist is available for use in the event of an alert being raised from IONM. This is especially important in centres where neuromonitoring is not routine, and/or where team members are unfamiliar with each other's practice. Such a checklist also acts as a training tool for trainees in all disciplines involved and may be used as a

medicolegal document to confirm adherence to standard troubleshooting protocols. An example checklist is given in Table 6-1.

Table 6-1. A sample checklist to manage acute loss of IONM signal.

General	**Anaesthetic**	**Neurophysiologic**	**Surgical**
Intra-operative pause: stop case and announce to the room	Optimise mean arterial pressure	Confirm status of anaesthetic agents with anaesthetist	Consider events just prior to signal loss and reversal where possible
Eliminate distractions such as music and unrelated conversations	Optimise haematocrit	Exclude neuromuscular blockade	Remove traction
Summon anaesthetist, neurophysiologist and nurse to attention	Optimise acid-base balance, oxygen delivery and CO_2 clearance	Check electrodes and connections	Remove distraction
Anticipate need for peri-operative imaging	Ensure normothermia	Determine pattern and timing of signal changes	Remove rods
	Discuss potential need for wake-up test	Check for any postural effects, especially in unilateral loss	Remove screws and probe
Revisit situation after rectifying all correctible measures: decide whether to proceed, abandon, or perform wake-up testing			Evaluate for spinal cord compression
			Imaging to assess implant placement

It is usually the role of the operating neurosurgeon to guide the team in a "surgical pause" to evaluate the cause of any changes in neuromonitoring. The initial review is targeted at the most common causes of false positive

monitoring, including verification of placement of stimulating and recording leads.

Cost-effectiveness of IONM

Neuromonitoring has undoubtedly added to the cost of spinal and neurosurgery. This is largely due to the capital investment in equipment required, need to employ physiologists skilled in its use, and the necessary increase in surgical times. Though IONM makes logical sense based on first principles, there remains a lack of high-quality evidence as to clinical benefit. This is often due to the difficulties of ethically justifying a randomised controlled trial in which a proportion of patients were to be deliberately denied such monitoring. Attempts to produce consensus statements on the use of IONM have been hampered by the current dearth of evidence, and so the use of neuromonitoring has been driven by factors such as surgical preference and sensitivity to medicolegal concerns.

Complications

Table 6-2 summarises possible complications or confounders associated with neuromonitoring, alongside solutions which can mitigate them.

Table 6-2. Common IONM concerns and potential mitigations.

Problem	**Solution**
Bite injuries on MEP stimulation	Meticulous placement of bite blocks
Significant patient movement	Use the lowest possible stimulating current; communicate with surgeon and anaesthetist prior to running MEPs
Inaccurate pulse oximetry and/or blood pressure measurement during SSEP stimulation on ipsilateral side	Communicate with anaesthetist; compare bilateral readings or pause stimulation intermittently to obtain accurate readings
Sharps injuries from IONM needles	Proper disposal of sharps, documentation of sites of needle placement, role allocation and checking of removal at end of surgery

Vascular injury	Anatomical knowledge in relation to needle placement, compressive tamponade on removal
Seizures	Defined protocol in place for termination of intra-operative seizures

Summary

- Intra-operative neuromonitoring is increasingly used in neurosurgery.
- Its use requires teamwork and collaboration between the neurophysiologist, surgeon and anaesthetist.
- The modalities chosen should be tailored to the patient and procedure.
- The use of checklists is recommended to troubleshoot alerts raised on neuromonitoring.
- High-level evidence for IONM is currently still lacking, and its use is largely driven by institutional experience and large case series.

References

Hilibrand, A. S., D. M. Schwartz, V. Sethuraman, A. R. Vaccaro, and T. J. Albert. 2004. "Comparison of transcranial electric motor and somatosensory evoked potential monitoring during cervical spine surgery." *Journal of Bone & Joint Surgery - American Volume* 86 (6):1248-53.

Merton, P. A., and H. B. Morton. 1980. "Stimulation of the cerebral cortex in the intact human subject." *Nature* 285 (5762):227.

Nash, C. L., Jr., R. A. Lorig, L. A. Schatzinger, and R. H. Brown. 1977. "Spinal cord monitoring during operative treatment of the spine." *Clinical Orthopaedics & Related Research* (126):100-5.

Rijs, K., M. Klimek, M. Scheltens-de Boer, K. Biesheuvel, and B. S. Harhangi. 2019. "Intraoperative Neuromonitoring in Patients with Intramedullary Spinal Cord Tumor: A Systematic Review, Meta-Analysis, and Case Series." *World Neurosurgery* 17:17.

CHAPTER 7

AWAKE SURGERY: ANAESTHETISTS' PERSPECTIVE

HOLLY JONES

Introduction

The anaesthetist has a major role to play in enabling reliable intra-operative neuromonitoring whilst ensuring a positive patient experience during awake craniotomy (AC). Meticulous planning, discussion and consensus involving the surgeon, the neurophysiologist, the anaesthetist and the nursing staff is paramount in these very complex cases; it is especially important to empower the patient to understand the process and his or her shared involvement.

In this chapter the anaesthetists' perspective is discussed in relation to the use of AC and neurophysiological monitoring during this procedure. The main aim of AC is to minimise the risk of neurological damage while maximising tumour resection. Intra-operative neuromonitoring (IONM) aims to make this process as safe as possible and prevent long-term morbidity. In cases where both AC and IONM are used, the anaesthetist must be experienced in each technique independently before attempting surgery where both are used together.

Anaesthetic consultation

The pre-operative visit by the anaesthetist for a patient undergoing AC should include a discussion on the impact of the neuromonitoring in addition to the standard pre-assessment. An explanation needs to be given to the patient about the additional monitoring that is being used and why, although this does not replace formal consent taken by the surgeon. A discussion about multiple puncture sites or bruises caused by the monitoring needle electrodes and where they might be found after surgery should occur.

Needle electrodes might need to be placed in less standard areas like the anus, penis, clitoris, eye or soft palate. Here it is important to fully explain why and what to expect postoperatively. This should be documented to protect the anaesthetist and surgical team from any allegations arising from misunderstanding of bruising or soreness during recovery. For example, if the patient is undergoing a foramen magnum decompression and they wake up with not only a sore head, but a painful anus, they might well wonder why anal sphincter needling had not been explained. Other relevant history would include any eye pathology if peri-bulbar needle electrodes are being placed. Any pre-existing muscle weakness or nerve damage is important for the whole team to be aware of. As all needle electrodes are placed after induction of general anaesthesia and removed before waking, a refusal for monitoring is unlikely, as increasing safety and improving outcome from surgery is the main objective.

Pre-operative planning

It is important for the surgeon booking the list to document the use of both AC and IONM as this usually adds an extra one to two hours to the operating time of a craniotomy for a space-occupying lesion (SOL). It allows the anaesthetic assistant to prepare the appropriate equipment, including total intravenous anaesthesia (TIVA) pumps and depth of anaesthesia (DOA) monitoring. The anaesthetic visit can also be specifically targeted for the whole procedure. The theatre staff can prepare the “patient awake” signs for the doors to alert visiting staff members such as speech therapists and physiotherapists entering the theatre during surgery.

In every AC and IONM case, the anaesthetist, physiologist and surgeon should discuss their plan and any specific needs for the case. An agreement on what is to be tested and where the electrodes are to be placed should be reached before the patient arrives. This avoids mistakes such as tongue electrodes being inserted into a patient requiring intra-operative speech testing. At the pre-operative checklist, the neuromonitoring will be confirmed with the team and patient. The consent form should include the use of IONM, and any sensitive needle electrode sites being used. Special thought should be given to monitoring placement in a patient having an intra-operative wake-up for surgical resection. Needle electrodes should not be placed in uncomfortable places that might distract the patient from verbal testing, such as the eye, anus or soft palate. Pre-existing weaknesses and deficits should be carefully assessed and documented by the surgical team and discussed with the neurophysiologist. The intra-operative IONM

readings will be affected by the patient's pre-operative status, and baseline function is essential when looking for signal changes.

If the patient needs neuromonitoring before anaesthesia or before positioning, the anaesthetic should be adapted accordingly. The author has found concurrent dexmedetomidine and remifentanil infusions to be an excellent analgo-sedative strategy for this scenario (Table 7-1). The IONM needles are very small and similar in size to acupuncture needles. Thus, they are not too uncomfortable to place in a mildly sedated patient. In the case of motor monitoring before and after general anaesthetic and positioning, a supraglottic airway device (SAD) would be suitable for the majority of patients. This avoids the need for neuromuscular blocking agents and permits immediate motor testing. In the rare situation where tracheal intubation is necessary, a short or medium duration neuromuscular blocking agent is used, along with train-of-four monitoring (TOF) and reversal agents where necessary. Usually, the neuromuscular blockade has worn off by the time of first motor testing, after patient positioning and placement of lines, catheters and needles. The use of sugammadex for immediate reversal of neuromuscular block for motor testing is reserved only for specific patients due to cost implications. This may change in the future if the cost of the drug reduces.

Table 7-1. Established drug combinations for induction of anaesthesia where there is a need for baseline IONM.

Drug	**Dilution**	**Dose range**	**Notes**
Dexmedetomidine	200 mg in 50 ml 0.9% NaCl (4 mcg/ml)	0.1-1.0 mcg/kg/hr	Bolus doses may be necessary (0.1mcg/kg over 3 mins, repeated 1-3 times over 10 mins)
Remifentanil	2 mg in 40 ml 0.9% NaCl (50mcg/ml)	0.1-0.2 mcg/kg/min	TCI pump needed
Propofol	2% (neat)	Induction dose reduces to maintenance dose	TCI pump needed; titrated to depth of anaesthesia monitor, minimised for optimal wake-up

Induction of anaesthesia

All Association of Anaesthetists (AoA) recommended monitoring (Checketts et al. 2016) should be placed prior to induction, including a DOA monitor. The propofol and remifentanil target-controlled infusion (TCI) dose appropriate for the patient should be chosen and started. The avoidance of any other longer-acting opiates for induction should lead to a short and predictable emergence. After placement of a SAD (the author finds the reinforced laryngeal mask airway (LMA) ideal in these patients), the invasive monitoring lines and IONM needles can be placed. Placing the anaesthetic vascular access and monitoring lines, urinary catheter and IONM needles simultaneously can reduce the set-up time significantly. If possible, the anaesthetic (venous/arterial) lines should be placed on the non-tested arm to avoid interference. In specific circumstances, all lines should be placed in the lower limbs if fine motor skills are being tested, for example, playing a musical instrument during the awake phase. During motor stimulation the arterial line and pulse oximeter traces usually display interference and read incorrectly. These can mimic serious cardiac arrhythmia (Figure 7-1) and also risk line displacement, so lines should be secured well. A scalp block can be performed under anaesthesia or sedation, and scalp pin sites injected with lidocaine and adrenaline. A good scalp block is vital to successful AC.

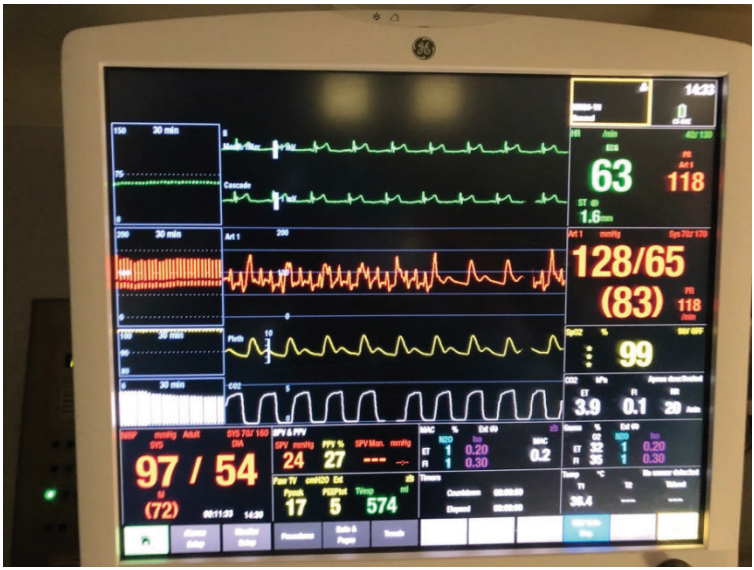

Fig. 7-1. MEP interference in the arterial line trace.

Depth of anaesthesia monitoring

All inhaled anaesthetic gases interfere with IONM, specifically MEPs, so should be avoided if possible. This is more challenging in very small children, in whom the risk-benefit balance should be assessed; small doses of volatile agents can reduce propofol requirement to mitigate the risk of propofol infusion syndrome.

TIVA is preferable for this surgery, and the addition of remifentanil to propofol avoids the need for any further neuromuscular blocking agents (NMBAs) after induction. However, it is important to ensure the plane of anaesthesia is not too deep, or the IONM will be affected and become unreliable. Too light a plane of anaesthesia should also be avoided in order to prevent awareness. Ensuring that the patient receives minimum sedative anaesthetic doses just before wake-up is optimal. This can be achieved by carefully titrating the propofol target down and increasing the dexmedetomidine under DOA monitoring. The remifentanil should be kept at an adequate dose to allow fully mandatory mechanical ventilation and tight $PaCO_2$ control (4.5-5.0 kPa).

The DOA monitor should be used in accordance with NICE guidance, which recommends – but does not insist on – its use with TIVA anaesthesia (NICE 2012); there are important limitations to the technique (Shepherd et al. 2013) (Pandit and Cook 2013). Bispectral Index (BIS), E-Entropy and Narcotrend have been compared in their ability to prevent awareness but none is considered superior to any other (Punjasawadwong, Boonjeungmonkol, and Phongchiewboon 2007) (Punjasawadwong, Phongchiewboon, and Bunchungmongkol 2014). DOA monitors may only offer a false sense of security (Myles et al. 2004) (Avidan et al. 2008) (Green 2016) and should be used alongside clinical information. The advantages and disadvantages of the two most popular kinds of DOA monitoring can be found in Table 7-2.

It has been argued that separate DOA monitoring is not necessary in addition to IONM, as the latter includes full electro-encephalography (EEG) and so is a more sophisticated monitor compared to any anaesthetic system currently available. However, it still remains the anaesthetist's role and responsibility to ensure that correct depth of anaesthesia is maintained, and therefore a familiar anaesthetic DOA system in close vicinity read and interpreted by the anaesthetist seems the logical solution. While interaction with the neurophysiologist about depth and adequacy of readings remains vital, it should be in addition to and not replacing the DOA controlled by

the anaesthetist. It would be difficult to argue in a medicolegal case that the neurophysiologist was responsible for a case of awareness or a complication from anaesthesia that was inappropriately deep.

Table 7-2. Depth of anaesthesia monitoring: advantages and disadvantages.

Device	Advantages	Disadvantages
Bispectral index (BIS)	Shows EEG trace, EMG as a graduated response and suppression ratio for burst-suppression	Slow resonance to changes in depth due to cautioning effect; EMG changes from SSEP and EMG stimulation can cause false over-reading
E-Entropy	Shows EEG trace with a choice of amplitude to aid interpretation; shows burst-suppression ratio; immediate readout of entropy and therefore fast response to changes; state entropy is not affected by EMG, so less affected by induced SSEPs and EMGs	Can be altered by interference from IONM, giving unreliable results

It is particularly helpful to see the EEG trace on the chosen DOA monitor to look for burst-suppression. The presence of this pattern usually indicates that the patient is over-anaesthetised; this makes the IONM difficult to interpret and the patient slow to wake up. The burst-suppression ratio will be zero at adequate surgical depth of anaesthesia and receives little or no interference from the IONM and surgical field. When simulated, MEPs create patient movement which is detected by the electromyography (EMG) strip on the frontalis muscle, leading to a falsely high DOA reading. Therefore, it is important to interpret DOA readings in conjunction with the prevailing surgical and IONM conditions.

To maintain reliable IONM it is the anaesthetist's responsibility to ensure normothermia (Kochs 1995) (Koht, Sloan, and Toleikis 2017). Hypothermia will lead to poor and unreliable IONM readings and the deleterious effects of hyperthermia are well-documented (Suarez 2006).

The maintenance of a steady and adequate blood pressure that is suitable for the specific patient and surgery is also vital for reliable IONM; large fluctuations and hypotension will cause interference. If IONM readings are affected during surgery, either through swelling or direct effects, there might be a benefit after discussion with the surgeon to induce hypertension in an attempt to maintain blood supply to the affected area. This might return

IONM readings or have a favourable effect on preventing postoperative disability.

Awake surgery

Anaesthesia for awake surgery may sound like an oxymoron, but it describes the challenging technique of keeping a patient safe, still, comfortable, and cooperative during an intra-operative phase of intentionally reduced anaesthetic depth. A "wake-up" technique is used for surgical monitoring when an eloquent area of brain, such as speech cortex or motor or sensory cortex, is surgically involved – especially on the patient's dominant side. The aim of the wake-up test is to improve the safety of the surgery in preventing postoperative deficits by limiting the resection margins when changes are found clinically during the procedure.

In general, the surgical episode is divided into three phases. Phase 1 is from "knife-to-skin" through to raising the bone flap and opening the dura. The anaesthesia provided for this phase affects the wake-up time for the next phase. Phase 2 is the testing and mapping of the tumour, and this is when the patient needs to be "awake". There is usually also some resection during this phase. The anaesthetic status during phase 3 should make little difference to the surgeon and the choice will depend on the patient's wishes (which might have changed during surgery), safety and other physiological conditions during the anaesthetic.

The anaesthetic technique (Table 7-3) is best decided jointly with the surgeon, but it is vital to have an accurate picture of what exactly is being done and the likely timings involved. It is also important to be able to evolve and change the plan safely if circumstances change intra-operatively.

Many anaesthetic techniques are suitable for waking a patient intra-operatively, but access to the airway is always very limited, with the head held in a Mayfield clamp and secured to the operating table. The brain will also be exposed and therefore any changing of head position, coughing or straining can be very dangerous. Many anaesthetists would use a reinforced LMA for the first asleep phase, as the wake-up is smoother. If a second sleep phase is being used, the anaesthetic technique chosen should not rely on the ability to intubate safely and swiftly if anything were to go wrong. Intubating a patient intra-operatively in this position would be very challenging and risky and best avoided if possible. Therefore, an LMA is often placed again, the author preferring an iGel, as its rigidity makes it

easier to place facing the patient, avoiding intrusion into or contamination of the surgical field.

Table 7-3. Potential anaesthesia sequences during "awake" neurosurgery (* denotes the author's preferred techniques, depending on patient and surgical conditions).

Sequence	Notes
Awake throughout	Simplest technique but requires careful patient selection
Asleep-awake-asleep	Traditional technique, being departed from with newer pharmacological agents
Asleep-awake-sedated*	Avoidance of second sleep phase prevents need for further airway instrumentation
Awake-awake-asleep	Leads to very fast and good quality testing during middle awake phase
Awake-awake-sedated	As above for good testing conditions and reducing airway manipulation in the third phase
Sedated-awake-sedated*	As above, but better tolerated during phase 1 when removing bone flap and opening dura

High-flow nasal oxygenation (HFNO) is the ideal oxygenation method for the awake and sedated phase of an AC. This system is quiet, provides warm and humidified oxygen, and is well-tolerated by patients. It should be placed before the surgeons prepare and sterilise the operating field, as the strap needs to go behind the head. HFNO can be started after the surgeons are ready for the anaesthetist to wake up the patient.

To optimise the intra-operative wake-up time and clear-headedness of the patient, the volume of propofol given during phase 1 should be kept to a minimum. As already stated, burst-suppression should be avoided on the DOA monitor, and the recorded depth should be kept at the "lighter" end of the spectrum for general anaesthesia (e.g. BIS/E-Entropy score of 50-55). Dexmedetomidine facilitates a lucid wake-up and so can be titrated up to allow the propofol dose to be reduced.

Upon instruction to wake up the patient, all infusions should either be turned off or reduced to a minimum. Ensure that emergency airway equipment is immediately available, as well as suction and an anaesthetic assistant present in theatre. As the patient wakes up, asking them to remove the LMA themselves can be useful to demonstrate their wakefulness and ability to

obey commands. The testing can start soon after this, when all parties involved are satisfied that the patient is adequately complying with instructions. Testing can be in the form of motor, sensory, visual or language mapping. The exact type or types used depends on the site of the lesion being resected.

During awake surgery careful attention should be taken to ensure a quiet environment within the theatre. Signs should be placed on all entry doors to inform staff of an "awake" case in progress. Doors should have silent closing mechanisms to avoid banging and minimise auditory disturbance. The number of people in the operating room should be limited, bearing in mind that it is popular surgery for trainee doctors, nurses and allied health professionals to watch (with patient consent). Having too many observers increases infection risk as well as noise level. All visitors in the room should be very clear where to stand and when to be silent.

If the patient develops pain during the awake phase, the local anaesthesia scalp block can be repeated over the specific area of pain, the remifentanil TCI can be increased, or simple analgesics such as paracetamol added. If the patient becomes restless or agitated during testing, the dexmedetomidine infusion may be increased. Sometimes the patient develops an unpleasantly dry mouth during testing, which can be alleviated with simple measures such as an oral foam swab dipped in water.

After awake testing is complete, the patient can either be re-anaesthetised, or have their sedation increased. If the former, the TCI propofol and remifentanil can be increased and an LMA then re-inserted. If the patient is to have only sedation, the dexmedetomidine and remifentanil can be increased and HFNO continued. End-tidal carbon dioxide can be difficult to monitor with this oxygen delivery system, so thoracic impedance is used to monitor respiratory rate (ensure that the alarms are set as appropriate).

Intra-operative IONM

Modalities

The evoked potential (response) is an electrical potential recorded from the nervous system following a stimulus. Spontaneous potentials are detected by EEG and EMG. Evoked potentials have a low amplitude, of the order of a few microvolts, compared to tens of microvolts for spontaneous EEG, millivolts for EMG, and close to a volt for ECG. Because of this low amplitude the somatosensory evoked potentials (SSEPs) need prolonged

averaging in order to be differentiated from noise. This can lead to a slow (3-5 minute) response to change during surgery.

SSEPs are recorded from the central nervous system after stimulation of sensory organs. They are typically achieved by stimulating the tibial, median or ulnar nerve, and recording responses at the scalp. The two most studied parts of the SSEP are the amplitude and latency of the peaks. These are referenced to the patient's baseline after induction of anaesthesia. An increase in latency and decrease in amplitude can indicate neurological dysfunction. Anaesthetic gases mimic this effect, making signal interpretation difficult, inaccurate or impossible. SSEPs monitor the dorsal column, which would be too painful to use in the awake patient.

Motor evoked potentials (MEPs) are performed by direct stimulation of the cortex or via transcranial stimulation. MEPs monitor the pyramidal tract or the lateral corticospinal tract. Since the ventral and dorsal columns have separate blood supplies it is often necessary to monitor both MEPs and SSEPs during surgery.

Practical aspects

Careful and safe patient positioning is vital for all neurosurgery and changes in IONM can come about from positioning that affects the blood supply to a nerve or causes direct pressure. Correct neck positioning is crucial to spinal cord perfusion as direct pressure from hyper-flexed or extended necks can lead to loss of spinal cord signals. If the neurophysiologist starts to lose signal over a period of minutes to hours, then repositioning should be considered. As obesity increases in the surgical population, safe positioning can be very challenging; the neurophysiologist can help reduce damage that occurs from positioning during surgery.

As with all neuro-anaesthesia, partial pressures of oxygen and carbon dioxide should be carefully maintained above 13 kPa and between 4.5-5.0 kPa respectively. This maintenance of the normal physiological state helps the neurophysiologist detect changes in the patient that are purely related to surgery. Low $PaCO_2$ is associated with vasoconstriction that can impair cerebral perfusion. High $PaCO_2$ and/or low PaO_2 can lead to vasodilation, cerebral oedema and raised intracranial pressure, especially in the presence of a large tumour. High PaO_2 can cause free radical formation and absorption atelectasis.

Normotension should be maintained and swings in blood pressure avoided. Hypotension can lead to lack of perfusion, which affects IONM. Hypertension risks intra-operative bleeding at critical sites. Normothermia should be maintained. Normoglycemia is vital for good outcomes in neurosurgery, as is optimal haemoglobin concentration for oxygen delivery to tissues.

Drugs affecting IONM

Table 7-4 describes the effect of various anaesthetic drugs on the main IONM modalities.

Table 7-4. Common anaesthetic drugs and their interactions with IONM.

Drug	Effect on MEP	Effect on SSEP
Neuromuscular blocking agents	Obliterate in a dose-dependent manner	No effect
Inhalational anaesthetic agents	Dose-dependent effect on latency and amplitude in even small concentration, obliterated at 1 MAC	Some dose-dependent effect
Thiopentone	Large effect in a dose-dependent manner, similar to volatile agents	Some dose-dependent effect
Benzodiazepines	Dose-dependent effect	Little or no effect at clinically used doses
Alpha-2 agonists (clonidine and dexmedetomidine)	Some dose-dependent effect	Little or no effect at clinically used doses
Magnesium	Some dose-dependent effect	Little or no effect at clinically used doses
Opiates, including remifentanil	Little or no effect at clinically used doses	Some dose-dependent effect, decreasing latency and amplitude
Propofol	Some decrease at clinically used levels, obliterated at high doses	Some dose-dependent effect, decreasing amplitude

Loss of IONM signals

The neurophysiologist should alert the surgeon and anaesthetist immediately, while ensuring that this is a true change and not a monitor problem. The anaesthetist should check for any anaesthetic cause (See Table 7-5). The decision on what action to take must result from a team discussion (Wing-hay and Chun-kwong 2019). This includes the decision of whether to proceed with, expedite or abandon surgery. A surgical pause may be appropriate to permit the correction of rectifiable issues and hopefully facilitate return of signals. Surgery may need to continue if at a vital stage, or if signals are lost when there is little risk of nerve damage (high probability of a false-positive alert). If going ahead, consider whether other actions need to be taken (for example, liaising with critical care for postoperative admission for hypertensive therapy or ongoing mechanical ventilation if the respiratory nerves are affected).

Table 7-5. Anaesthetic causes of loss of IONM signal.

Cause	**Management**
Hypothermia	Warm patient, but be mindful that blood >37°C entering the brain can have an adverse effect on outcome
Hypotension	Increase BP with fluids and/or vasoconstrictors, guided by clinical signs and monitoring; check lactate and base deficit and watch trends; consider cardiac output monitoring
Anaemia	Transfuse packed red cells if Hb <90g/l intra-operatively; be aware of temperature at which blood products are delivered, and the risk of hyperkalaemia and hypocalcaemia which accompanies transfusion
Hypoxaemia	Treat the cause (e.g. tracheal tube endobronchial displacement, bronchospasm, pneumothorax (the latter is possible in cervical and thoracic surgery)); increase FiO_2, minute volume and/or PEEP (recognising that increased intrathoracic pressure transmits to intracranial and intraspinal pressure); serial arterial blood gases; consider on-table CXR; ensure hypotension and anaemia are not contributing to hypoxaemia
Hypocarbia	Exclude venous air embolism and activate air embolism drill if suspected; address hypotension and hypoperfusion as contributory causes; adjust ventilation to achieve normocarbia based on arterial blood gas $PaCO_2$ (do not rely on end tidal CO_2)

Incorrect depth of anaesthesia	Refer to anaesthesia monitor and/or discuss with neurophysiologist on their reading of the patient's depth on EEG; titrate anaesthetic agents appropriately to avoid burst-suppression
Incorrect positioning causing nerve ischaemia	This may be a diagnosis of exclusion; typically, IONM signals begin to fade after about an hour with no other cause found; sometimes small adjustments to neck or back position may cause a fast improvement to signals
Drug administration (either inadvertent or unavoidable)	This might be a drug given in error (e.g. a neuromuscular blocking agent) or a drug needed to treat an anaesthetic issue (e.g. magnesium to treat an arrhythmia); discuss with the neurophysiologist before and after giving the drug to enable them to accurately interpret the responses; if a drug needs to be given to maintain patient safety then it should not be omitted simply because of its effects on IONM

Postoperative care

All IONM needle electrodes must be removed at the end of surgery and disposed of in a sharps bin. This is the responsibility of the person who placed them (usually the neurophysiologist). Any areas that are excessively bleeding will need either pressure dressings or surgical attention. The recovery (or critical care) nurse needs to be informed about the use of IONM and where the needle electrodes were placed so that they can watch for any bleeding problems and remind the patient about why they are there. Long-term sequelae from IONM are unusual, but there is some anecdotal evidence of memory loss. More research is required in this area.

References

Avidan, M. S., L. Zhang, B. A. Burnside, K. J. Finkel, A. C. Searleman, J. A. Selvidge, L. Saager, M. S. Turner, S. Rao, M. Bottros, C. Hantler, E. Jacobsohn, and A. S. Evers. 2008. "Anesthesia awareness and the bispectral index." *New England Journal of Medicine* 358 (11):1097-108.

Checketts, M. R., R. Alladi, K. Ferguson, L. Gemmell, J. M. Handy, A. A. Klein, N. J. Love, U. Misra, C. Morris, M. H. Nathanson, G. E. Rodney, R. Verma, J. J. Pandit, Britain Association of Anaesthetists of Great, and Ireland. 2016. "Recommendations for standards of monitoring during anaesthesia and recovery 2015: Association of Anaesthetists of Great Britain and Ireland." *Anaesthesia* 71 (1):85-93. doi: 10.1111/anae.13316.

Green, N. H. 2016. "To BIS or not to BIS." *British Journal of Anaesthesia* 116 (5):726-7.

Kochs, E. 1995. "Electrophysiological monitoring and mild hypothermia." *Journal of Neurosurgical Anesthesiology* 7 (3):222-8.

Koht, A., T.B. Sloan, and J.R. Toleikis. 2017. *Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals*. Edited by A. Koht, T.B. Sloan and J.R. Toleikis. 2nd Edition ed. Chicago, U.S.A.: Springer.

Myles, P. S., K. Leslie, J. McNeil, A. Forbes, and M. T. Chan. 2004. "Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial." *Lancet* 363 (9423):1757-63.

NICE. 2012. Depth of anaesthesia monitors – Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M. In *DG6*. London: National Institute for Health and Care Excellence.

Pandit, J. J., and T. M. Cook. 2013. "National Institute for Clinical Excellence guidance on measuring depth of anaesthesia: limitations of EEG-based technology." *British Journal of Anaesthesia* 110 (3):325-8.

Punjasawadwong, Y., N. Boonjeungmonkol, and A. Phongchiewboon. 2007. "Bispectral index for improving anaesthetic delivery and postoperative recovery." *Cochrane Database of Systematic Reviews* (4):CD003843.

Punjasawadwong, Y., A. Phongchiewboon, and N. Bunchungmongkol. 2014. "Bispectral index for improving anaesthetic delivery and postoperative recovery." *Cochrane Database of Systematic Reviews* (6):CD003843.

Shepherd, J., J. Jones, G. Frampton, J. Bryant, L. Baxter, and K. Cooper. 2013. "Clinical effectiveness and cost-effectiveness of depth of anaesthesia monitoring (E-Entropy, Bispectral Index and Narcotrend): a systematic review and economic evaluation." *Health Technology Assessment (Winchester, England)* 17 (34):1-264.

Suarez, Jose I. M. D. 2006. "Outcome in neurocritical care: Advances in monitoring and treatment and effect of a specialized neurocritical care team." *Critical Care Medicine Critical Care Challenges in Special Patient Populations* 34 (9):S232-S238.

Wing-hay, H.Y., and E.C. Chun-kwong. 2019. "Introduction to Intraoperative Neurophysiological Monitoring for Anaesthetists." World Federation Of Societies of Anaesthesiologists, accessed 21st April 2019. www.wfsahq.org.

CHAPTER 8

IMPLICATIONS OF GENERAL ANAESTHESIA

ROBIN KUMAR
CHULANANDA GOONASEKERA

Introduction

Intra-operative neurophysiological monitoring (IONM) analyses the functional integrity of selected neural structures during surgery (Sala 2010) (Stecker 2012). The purpose is to reduce the risk of iatrogenic neurological damage by identifying potential injury at reversible stages. IONM is generally considered safe and is increasingly used in adult and paediatric neurosurgical procedures (Soghomonyan et al. 2014) (Coppola et al. 2016) (Rho, Rhim, and Kang 2016); many centres routinely use IONM for complex brain and spinal cord surgeries. Most neurosurgeons consider the technique an important tool to minimise risk in neurosurgery (Cabraja et al. 2009). Though not a new development, IONM has become increasingly sophisticated, with improvements in software and surgical technology combined with improved imaging, neuroanaesthesia and postoperative care.

Correct signal interpretation is key for reliable IONM, and this requires knowledge of neurophysiology, the surgical procedure, and the effects of general anaesthesia. A team approach is essential to obtain meaningful results.

Operating theatre preparation

Setting up IONM in the operating theatre usually occurs after the induction of general anaesthesia. Corkscrew electrodes are inserted into the scalp at designated points linked to the topographical location of brain structures (e.g. primary motor cortex, sensory cortex). Needle electrodes may be implanted into the spine, limbs, tongue, oropharynx, eyes, ears, face, genitals and anus (Legatt et al. 2016). The placement of these electrodes varies depending on the type of surgery and IONM modality to be used. The electrodes permit the neurophysiologist to stimulate and record evoked potentials, whilst also monitoring the spontaneous electrical activity of the brain (Liem 2016). The surgical team and neurophysiologist co-interpret the triggered and spontaneous electrophysiological signals from the patient throughout the course of the operation.

The interactive software running on the IONM computer system carries out three core tasks: selective activation of stimulating electrodes with appropriate timing; processing of the electrophysiological signals; and displaying an output. The neurophysiologist observes and documents the output in real time.

Electrode displacement, wire disconnection, and electromagnetic interference are common causes of lost or distorted signals. It is essential to keep all connections tidy to minimise entanglement with surgical and anaesthetic equipment and avoid false alerts during surgery.

IONM modalities

There are numerous modalities of IONM. Several are often used together in a single operation as each modality provides unique information (Kim et al. 2013). A summary of commonly used modalities is shown in Table 8-1.

Table 8-1. Modalities of IONM.

Modality	**Summary**	**Anaesthetic interactions**
Motor Evoked Potentials (MEPs)	MEPs are obtained by magnetic or transcranial electrical stimulation, or by direct stimulation of the motor cortex (Kim et al. 2013). MEPs examine the integrity of the motor pathway by recording the resultant muscular contractions from peripherally placed (e.g. hand, foot) needle electrodes. MEPs can only be assessed periodically during surgery, which raises the possibility of delays in identifying neurological damage. Generally, MEPs are monitored together with SSEPs during intracranial and spinal surgery.	MEPs are affected by volatile anaesthetic agents, and so in general, total intravenous anaesthesia (TIVA) is used. However, inhalational agents at 0.5 Minimum Alveolar Concentration (MAC) or below may still occasionally be used, especially in intracranial surgery. MEPs activate the muscles of mastication. A soft bite block must be placed to minimise the risk of tongue, lip and dental damage.
Somatosensory Evoked Potentials (SSEPs)	SSEPs are the most commonly used evoked potential modality. They represent recordings of ascending sensory signals that monitor the dorsal column-medial lemniscus pathway (Lall et al. 2012). Stimulating electrodes are frequently placed over the median and ulnar nerve in the upper limbs, and the posterior tibial nerves in the lower limbs (Lall et al. 2012) (Busso and McAuliffe 2014). Signals are recorded via the scalp. Unlike MEPs, SSEPs can be monitored continuously throughout surgery (Lall et al. 2012).	Adequate SSEPs can usually be recorded at 0.5 to 1 MAC of volatile agent. However, for patients with any degree of baseline neurologic impairment, even low levels of inhalation agents may abolish potentials and make monitoring impossible.

Electro-encephalography (EEG)	EEG records brain electrical activity using corkscrew needles placed in the post-central parietal regions of the scalp (Kim et al. 2013). It provides a functional assessment of the cerebral cortex, and can detect ischaemia, seizure activity, and depth of anaesthesia. EEG is commonly used during carotid endarterectomy to assess cerebral perfusion during carotid cross-clamping.	Many anaesthetic agents reduce EEG activity; this is the basis of depth of anaesthesia monitors.
Electrocorticography (ECoG)	ECoG is recorded by an electrode strip placed directly over the surface of the brain by the surgeon. These recordings may assist in the location of an epileptic focus on the motor gyrus. EEG and ECoG recordings can be discordant; for example, when EEG signals are very poor or absent, ECoG signals may persist.	Many anaesthetic agents have an effect on epileptiform activities.
Electromyography (EMG)	In spontaneous EMG, needle electrodes are placed in certain muscle groups and activity is monitored continuously without electrical stimulation of the corresponding nerve. Triggered EMG involves stimulation of the relevant nerve (cranial, spinal or peripheral), and assessment of the recordings at muscle level (e.g. facial nerve monitoring during parotid surgery). Combining spontaneous and triggered EMG is an effective way to anticipate and minimise damage to nerves (Lall et al. 2012).	Both EMG and MEPs are abolished by neuromuscular blocking agents.

Brainstem Auditory Evoked Potentials (BAEPs)	BAEPs are generated by auditory stimulation of the vestibulocochlear nerve (cranial nerve VIII). This can minimise the risk of nerve damage and subsequent hearing loss (Kim et al. 2013). Several variants of this monitoring exist (Rosengren, McAngus Todd, and Colebatch 2005). BAEPs are primarily used in posterior fossa surgery. They can be unreliable and difficult to detect.	Compared with other IONM modalities, BAEPs are very resistant to anaesthetic agents.
Visual Evoked Potentials (VEPs)	VEPs assess the integrity of the visual pathway. A device that produces flashes of light is placed over the closed eyelid. On average one flash per second is used, and the intensity of the flash can be varied. Electrical potentials generated by these brief visual stimuli are recorded via scalp electrodes.	VEPs are sensitive to inhalational anaesthetics.
D-Waves	Stimulation of the pyramidal and internuncial cells in the brain generates D (direct) waves, recorded from the epidural space (Kim et al. 2013).	D-waves are minimally affected by anaesthetic agents.

For any given operation, the choice of modalities depends on which neural structures are at risk. There are some existing regional guidelines that recommend certain modalities of monitoring (Macdonald et al. 2013) (Dionigi et al. 2013). However, the methods used are often dependent on the experience and understanding of the surgeon, anaesthetist and neurophysiologist and their functionality as a team (Jameson, Janik, and Sloan 2007). There is therefore a great deal of variation in practice between institutions. The following are some examples of how IONM is used in specific types of surgery.

Spinal surgery

Peri-operative spinal cord injury is one of the most feared complications of spinal surgery. A systematic review reported that multimodal IONM is sensitive and specific in its detection of intra-operative neurological injury during spinal surgery (Fehlings et al. 2010); however, there is a need to develop evidence-based protocols to manage intra-operative changes in IONM, and to validate these prospectively. Another systematic review found that all cases of paraparesis, paraplegia, and quadriplegia occurred with corresponding electrophysiological changes, with none occurring without signal change (Nuwer et al. 2012). A single-centre study reviewing the practice of spinal surgeons recommended the development of practice guidelines for specific procedures (Rattenni et al. 2015).

For spinal surgery, MEPs, SSEPs and EMGs are generally combined to monitor spinal cord function in order to increase sensitivity. MEPs are monitored periodically throughout surgery, and a decrease in amplitude is a more sensitive sign of impending neurological compromise than an increase in latency.

Vascular surgery

Patients undergoing carotid endarterectomy are at risk of a reduction in cerebral blood flow and embolic episodes. EEG and SSEP monitoring is therefore often used in this clinical scenario.

Surgical repair of descending thoracic and thoraco-abdominal aortic aneurysms is another vascular procedure in which IONM may be implemented. A European study assessing the use of IONM in such procedures concluded that it is both feasible and effective as an adjunct to spinal cord protection (Greiner et al. 2012).

Thyroid surgery

The National Institute for Health and Care Excellence (NICE) published guidelines on intra-operative nerve monitoring during thyroid surgery in 2007 (NICE 2008). During such procedures, the recurrent laryngeal nerve may be inadvertently damaged, leading to hoarseness, stridor and respiratory distress due to vocal cord palsy. However, the evidence for IONM in this situation is conflicting and its absolute value during thyroid surgery is yet to be established (Gardner, Doherty, and McAneny 2016).

Anaesthesia and IONM

All anaesthetic agents directly interfere with IONM signal quality to some degree. Modes of evoked responses that travel via pathways with a greater number of synapses, such as VEPs, are more vulnerable to signal interference; D-waves, conversely, do not involve any synapses and hence are considered highly reliable even in the presence of anaesthetic agents (Soghomonyan et al. 2014). For most modalities therefore, major modifications to general anaesthesia are required to produce accurate readings (Cabraja et al. 2009) and it is important for the neurophysiologist to be aware which agents are being administered. Additionally, administration of drugs in bolus doses, and variations in the depth of anaesthesia (DOA), can cause signal suppression indistinguishable from changes triggered by surgical trauma (Lotto, Banoub, and Schubert 2004). On the whole, anaesthetic-related changes tend to globally affect IONM signals, whereas surgical factors lead to more focal changes.

EEG changes

Inhalational anaesthetic agents, thiopental, and propofol all produce anaesthesia in part by potentiating inhibitory $GABA_A$ receptors. Although each class of agent tends to produce its own characteristic EEG waveform, all undergo similar changes as the concentration of administered anaesthetic increases. In the lighter planes of general anaesthesia, amplitude is shallow, and frequency high. As anaesthetic depth increases, the amplitude deepens, and frequency slows. During deep anaesthesia, a typical burst-suppression pattern emerges, characterised by alternating episodes of high-frequency, large-amplitude waves (bursts) and flat traces (suppression). Beyond this, flat traces predominate, resulting in an iso-electric EEG. The major difference in the EEG between the volatile agents and propofol is power in the theta range. In propofol TIVA, theta power remains low regardless of drug concentration, but in the presence of isoflurane or sevoflurane, it rises. Alpha oscillations (around 10 Hz) are often seen when a person is awake with their eyes closed; such oscillation is mostly observed in the occipital regions. Conversely, alpha rhythms during both surgical anaesthesia and normal sleep are mostly seen in the frontal regions. This is known as anteriorisation of the alpha rhythm and is common with all anaesthetic agents (Hagihira 2015).

Inhalational anaesthetic agents

Volatile halogenated inhalational anaesthetics (such as isoflurane, sevoflurane, desflurane, and historically, halothane) cause a dose-dependent reduction in amplitude and rise in latency of the evoked responses, to varying degrees. Their effects are much greater on cortical as opposed to subcortical responses. The effect of nitrous oxide on IONM is similar to that of the volatile inhalational agents and is synergistic when co-administered with them. MEPs are very sensitive to volatile agents; SSEPs are moderately affected; and BAEPs are relatively resistant.

Except for halothane, the volatile agents produce an initial increase in the frequency of the frontal EEG, with a decrease in frequency and amplitude at higher doses. Burst-suppression occurs at approximately 1.5 Minimum Alveolar Concentration (MAC), giving way to electrical silence at even higher doses. Sevoflurane can produce seizure activity with the high doses associated with inhalational induction of anaesthesia.

Intravenous anaesthetic agents

Intravenous anaesthetic agents have reduced suppressant effects on electrical signals compared to inhalational agents (Banoub, Tetzlaff, and Schubert 2003), although will also ultimately produce burst-suppression and electrical silence at high doses. While propofol does decrease the amplitude of cortical evoked potentials, monitoring of evoked potentials in neurologically intact patients is usually still possible at clinically relevant doses. Therefore, particularly in adults, the most common anaesthetic technique used for IONM is total intravenous anaesthesia (TIVA) with propofol (often delivered as a target-controlled infusion [TCI]), in combination with a potent opioid (typically a remifentanil infusion), titrated to effect using DOA monitoring (Soghomonyan et al. 2014). This may be supplemented by other intravenous narcotic and sedative agents based on clinician preference.

In children, propofol and remifentanil infusions are sometimes combined with low-dose inhalational agents. Sevoflurane has relatively low solubility and is thus eliminated rapidly. Using sevoflurane as an induction agent, Fulkerson and colleagues demonstrated the successful use of IONM in young children undergoing spinal procedures (Fulkerson et al. 2011). The addition of 0.3 to 0.5 MAC of an inhalational agent allows reduction of the dose of propofol infusion; this reduces the risk of propofol infusion syndrome,

facilitates more rapid emergence and earlier neurologic examination, and may reduce the incidence of awareness under general anaesthesia.

Neuromuscular blocking agents

Neuromuscular blocking agents (NMBAs) are avoided during monitoring of MEPs and EMGs due to their severe attenuation of the signal. In general, an NMBA is administered during induction of general anaesthesia to facilitate tracheal intubation. By the time the patient has been prepared for surgery (following further anaesthetic preparation, application of electrodes and patient positioning), the neuromuscular blockade has usually worn off and the neurophysiologist can record meaningful MEPs and EMGs.

There may be specific situations, however, where baseline MEPs are requested immediately following tracheal intubation (e.g. in the case of an unstable cervical spine). This may be facilitated by the avoidance of NMBAs (e.g. via the administration of high doses of potent, rapidly acting opioids such as alfentanil), or rapid reversal of the NMBA (e.g. reversing rocuronium with sugammadex).

It is possible to record MEPs with a low residual level of neuromuscular blockade (e.g. two out of four twitches with train-of-four peripheral nerve stimulation). In practice it may be difficult to achieve a constant level of neuromuscular blockade.

Opioid analgesics

Opioids cause mild dose-dependent depression of SSEP and MEP responses; even at very high doses, evoked potentials can still be recorded. The mild suppressive effects of opioids are proportional to their lipophilicity. Infusions of remifentanil at high doses (0.2 to 0.5 mcg/kg/min) are commonly used as part of TIVA during IONM.

Other anaesthetic agents

SSEPs and MEPs are unaltered by benzodiazepines at low doses; such drugs are anticonvulsant and produce EEG slowing, but not usually burst-suppression or electrical silence.

SSEPs are unaffected by barbiturates (e.g. sodium thiopental, pentobarbital) even at very high doses. However, MEPs *are* sensitive to this drug class, with effects lasting beyond the duration of anaesthetic effect.

Ketamine enhances the amplitude of cortical SSEPs and MEPs, meaning that a ketamine infusion may occasionally be beneficial during the use of IONM. Ketamine may however lower the seizure threshold in patients with epilepsy.

Etomidate increases the amplitude of cortical SSEP recordings, an effect that may be useful to the neurophysiologist. Etomidate can provoke seizure activity in patients with epilepsy and has been used with ECoG to locate seizure foci. The use of etomidate is limited by its association with adrenal suppression (even after a single dose) and worsened outcomes in sepsis.

Dexmedetomidine infusions may be used when recording SSEPs or MEPs. However, high doses may attenuate MEP signals.

Intravenous lidocaine can be a useful anaesthetic adjunct due to its ability to reduce anaesthetic requirements and stabilise cardiovascular parameters.

During lengthy neurosurgical procedures, gradual attenuation of the electrophysiological signal may occur. This signal degradation is not necessarily related to the dose of anaesthetic agents and is proportional to the duration of anaesthesia. The phenomenon is seen more often in younger patients, and those with spinal cord pathology. The exact mechanisms underlying such signal degradation are currently not well understood.

Physiological factors

A reduction in systemic or regional blood pressure can affect IONM signals. It is therefore advisable to target as close to normotension as possible. Even at normal mean arterial pressures, local factors (e.g. spinal distraction, vascular compromise from positioning, retractor pressure) may result in ischaemia and corresponding IONM changes. In addition, patients with abnormal cerebral or spinal perfusion or autoregulation at baseline (e.g. hypertension or vasculopathy) are at higher risk of ischaemia with any disturbance of blood flow. Thus, when IONM changes occur, an induced rise in mean arterial pressure may be required to maintain tissue perfusion pressure.

Changes in the partial pressures of oxygen (PaO_2) and carbon dioxide ($PaCO_2$) can affect IONM either by alteration of oxygen delivery or changes in blood flow, especially in patients with compromised vascular anatomy. However, these effects only tend to be seen at extremes of PaO_2 and $PaCO_2$.

Lowered core body temperature has been shown to alter EEG, SSEPs, BAEPs, VEPs and MEPs, in general globally increasing signal latency. Therefore, it is important to maintain normothermia. Localised hypothermia (e.g. due to exposure of the surgical site) can also affect IONM signals but produces more focal changes.

Anaemia can affect IONM (both amplitude and latency) by either reducing oxygen-carrying capacity or changing the rheology of blood.

Patient positioning

Patient positioning for surgery can cause neurologic and/or vascular compromise and can therefore affect IONM.

In cases where extreme neck flexion is required (e.g. cervical spine or posterior fossa surgery), baseline MEPs and SSEPs are performed after induction of general anaesthesia with the patient supine, and then again after positioning. If recorded potentials deteriorate between these stages, changes to position can be made before surgery begins, or consideration given to a wake-up test.

IONM changes can occur later on during surgery if limbs are moved or shoulders sag, or because of pressure on peripheral nerves.

Important considerations

There exists an increased risk of awareness with TIVA, due to the possibility of intravenous line disconnection or infusion pump failure; intravenous drug levels are only ever *calculated* by TIVA pumps, as opposed to end-tidal anaesthetic agents being *measured* in inhalational anaesthesia. It is therefore prudent to use a DOA monitor, particularly if NMBAs are used. Bispectral index (BIS) is the most frequently used DOA monitor at present. It displays a scale from 0 to 100, with general anaesthesia typically being achieved with values between 40 and 60. Values of 60 to 80 represent sedation, and those above 80 indicate increasing levels of consciousness. Values below 40 correlate with

increasing EEG suppression. Anaesthetists can use this information to titrate the doses of anaesthetic agents (Bruhn et al. 2006).

Some IONM electrodes are placed in areas that restrict important access for the anaesthetist (e.g. electrodes placed in the soft palate and tongue may limit access to the airway). It is important to discuss electrode placement with the neurophysiologist before the patient arrives.

Signal loss

When an IONM alert occurs, surgical, anaesthetic, physiological, positional, and technical causes must be investigated using a team approach. Differentiating signal changes along these lines is the joint task of the triad of surgeon, anaesthetist, and neurophysiologist. When encountered, IONM changes may be reconfirmed by another signal acquisition (if time allows) before a call for action is initiated. Depending on the monitoring modality in use, the differential diagnosis may be narrowed down by identifying the change as cortical versus subcortical, unilateral versus bilateral, and/or focal versus global. In general, surgical, technical, and positional aetiologies result in localised changes, whereas anaesthetic and physiological factors tend to have more global effects on IONM signal. At certain stages of surgery, there may be an obvious time-related cause for the change in IONM signal; prompt action may be necessary to avoid neurological injury.

Physiological causes (e.g. hypoxaemia, hypotension, hypothermia, anaemia), positional factors (e.g. extreme head position, peripheral nerve compression, spinal flexion or extension) and technical issues (e.g. lead failure or dislodgement, electrical interference, inaccurate electrode placement) must be considered as the potential causes of IONM signal change. Anaesthesia-related changes in evoked potentials may be more pronounced on the side of pre-existing asymmetric neurologic deficits (e.g. nerve root compression or unilateral spinal cord pathology).

While the cause is being investigated, the anaesthetist can help to minimise potential neurological injury by optimising physiological variables (e.g. raise blood pressure if appropriate, increase fraction of inspired oxygen, fluid resuscitation). Further treatment depends upon the identified cause and the individual clinical situation.

Summary

Evidence-based guidelines for the safe and efficacious implementation of IONM are lacking; the NICE guidelines refer only to thyroid surgery and arguably require updating. The use of IONM is therefore largely driven by surgeon preference, institutional experience, and medicolegal concerns.

Communication between the surgeons, anaesthetists and neurophysiologists is necessary for the successful application and interpretation of IONM. Pre-operative discussion should take place between these professionals, but in practice this is variable and unstandardised (Lall et al. 2012).

Clinicians involved require knowledge of the surgical procedure, neurophysiology and the effects of general anaesthesia on IONM (Stecker 2012). Anaesthetic technique typically involves the use of TIVA, avoidance of NMBAs (except at induction of general anaesthesia), and utilisation of a DOA monitor. The maintenance of stable physiological conditions is paramount. Any changes in IONM signal should prompt a concerted team effort to identify and treat the cause.

References

Banoub, M., J. E. Tetzlaff, and A. Schubert. 2003. "Pharmacologic and physiologic influences affecting sensory evoked potentials: implications for perioperative monitoring." *Anesthesiology* 99 (3):716-37.

Bruhn, J., P. S. Myles, R. Sneyd, and M. M. Struys. 2006. "Depth of anaesthesia monitoring: what's available, what's validated and what's next?" *British Journal of Anaesthesia* 97 (1):85-94.

Busso, V. O., and J. J. McAuliffe. 2014. "Intraoperative neurophysiological monitoring in pediatric neurosurgery." *Paediatric Anaesthesia* 24 (7):690-7.

Cabraja, M., F. Stockhammer, S. Mularski, O. Suess, T. Kombos, and P. Vajkoczy. 2009. "Neurophysiological intraoperative monitoring in neurosurgery: aid or handicap? An international survey." *Neurosurgical Focus* 27 (4):E2.

Coppola, A., V. Tramontano, F. Basaldella, C. Arcaro, G. Squintani, and F. Sala. 2016. "Intra-operative neurophysiological mapping and monitoring during brain tumour surgery in children: an update." *Childs Nervous System* 32 (10):1849-59.

Dionigi, G., F. Y. Chiang, H. Dralle, L. Boni, S. Rausei, F. Rovera, E. Piantanida, A. Mangano, M. Barczynski, G. W. Randolph, R. Dionigi,

and C. Ulmer. 2013. "Safety of neural monitoring in thyroid surgery." *International Journal Of Surgery* 11 Suppl 1:S120-6.

Fehlings, M. G., D. S. Brodke, D. C. Norvell, and J. R. Dettori. 2010. "The evidence for intraoperative neurophysiological monitoring in spine surgery: does it make a difference?" *Spine* 35 (9 Suppl):S37-46.

Fulkerson, D. H., K. B. Satyan, L. M. Wilder, J. J. Riviello, S. A. Stayer, W. E. Whitehead, D. J. Curry, R. C. Dauser, T. G. Luerssen, and A. Jea. 2011. "Intraoperative monitoring of motor evoked potentials in very young children." *Journal of Neurosurgery* Pediatrics.. 7 (4):331-7.

Gardner, I. H., G. M. Doherty, and D. McAneny. 2016. "Intraoperative nerve monitoring during thyroid surgery." *Current Opinion in Endocrinology, Diabetes & Obesity* 23 (5):394-9.

Greiner, A., W. H. Mess, J. Schmidli, E. S. Debus, J. Grommes, F. Dick, and M. J. Jacobs. 2012. "Cyber medicine enables remote neuromonitoring during aortic surgery." *Journal of Vascular Surgery* 55 (5):1227-32; discussion 1232-3.

Hagihira, S. 2015. "Changes in the electroencephalogram during anaesthesia and their physiological basis." *British Journal of Anaesthesia* 115 Suppl 1:i27-i31.

Jameson, L. C., D. J. Janik, and T. B. Sloan. 2007. "Electrophysiologic monitoring in neurosurgery." *Anesthesiology Clinics* 25 (3):605-30, x.

Kim, S. M., S. H. Kim, D. W. Seo, and K. W. Lee. 2013. "Intraoperative neurophysiologic monitoring: basic principles and recent update." *Journal of Korean Medical Science* 28 (9):1261-9.

Lall, R. R., R. R. Lall, J. S. Hauptman, C. Munoz, G. R. Cybulski, T. Koski, A. Ganju, R. G. Fessler, and Z. A. Smith. 2012. "Intraoperative neurophysiological monitoring in spine surgery: indications, efficacy, and role of the preoperative checklist." *Neurosurgical Focus* 33 (5):E10.

Legatt, A. D., R. G. Emerson, C. M. Epstein, D. B. MacDonald, V. Deletis, R. J. Bravo, and J. R. Lopez. 2016. "ACNS Guideline: Transcranial Electrical Stimulation Motor Evoked Potential Monitoring." *Journal of Clinical Neurophysiology* 33 (1):42-50.

Liem, L.K. 2016. Intraoperative Neurophysiological Monitoring. Medscape.

Lotto, M. L., M. Banoub, and A. Schubert. 2004. "Effects of anesthetic agents and physiologic changes on intraoperative motor evoked potentials." *Journal of Neurosurgical Anesthesiology* 16 (1):32-42.

Macdonald, D. B., S. Skinner, J. Shils, C. Yingling, and Monitoring American Society of Neurophysiological. 2013. "Intraoperative motor evoked potential monitoring - a position statement by the American

Society of Neurophysiological Monitoring." *Clinical Neurophysiology* 124 (12):2291-316.

NICE. 2008. Intraoperative nerve monitoring during thyroid yroid surgery. edited by National Institute for Health and Care Excellence. Manchester: National Institute for Health and Care Excellence.

Nuwer, M. R., R. G. Emerson, G. Galloway, A. D. Legatt, J. Lopez, R. Minahan, T. Yamada, D. S. Goodin, C. Armon, V. Chaudhry, G. S. Gronseth, C. L. Harden, Therapeutics, Neurology Technology Assessment Subcommittee of the American Academy of, and Society American Clinical Neurophysiology. 2012. "Evidence-based guideline update: intraoperative spinal monitoring with somatosensory and transcranial electrical motor evoked potentials: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the American Clinical Neurophysiology Society." *Neurology* 78 (8):585-9.

Rattenni, R. N., T. Cheriyan, A. Lee, J. A. Bendo, T. J. Errico, and J. E. Goldstein. 2015. "Intraoperative Spinal Cord and Nerve Root Monitoring: A Hospital Survey and Review." *Bulletin of the Hospital for Joint Disease* 73 (1):25-36.

Rho, Y. J., S. C. Rhim, and J. K. Kang. 2016. "Is intraoperative neurophysiological monitoring valuable predicting postoperative neurological recovery?" *Spinal Cord* 54 (12):1121-1126.

Rosengren, S. M., N. P. McAngus Todd, and J. G. Colebatch. 2005. "Vestibular-evoked extraocular potentials produced by stimulation with bone-conducted sound." *Clinical Neurophysiology* 116 (8):1938-48.

Sala, F. 2010. "Intraoperative neurophysiology is here to stay." *Childs Nervous System* 26 (4):413-7.

Soghomonyan, S., K. R. Moran, G. S. Sandhu, and S. D. Bergese. 2014. "Anesthesia and evoked responses in neurosurgery." *Frontiers in Pharmacology* 5:74.

Stecker, M. M. 2012. "A review of intraoperative monitoring for spinal surgery." *Surgical neurology international* 3 (Suppl 3):S174-87.

CHAPTER 9

DEPTH OF ANAESTHESIA MONITORING

CATALINA STENDALL
SARAH NOUR

Introduction and historical methods

The level of consciousness is assessed by the way in which we do or do not respond to a particular stimulus. We are regarded as being fully conscious when we respond to verbal stimuli. When there is no response to speech, or immobility as a result of a hypnotic or narcotic agent (as in anaesthesia), this represents increasing degrees of unconsciousness, especially when there is no response to a constant painful stimulus. This state of consciousness is judged as sufficient "depth" of anaesthesia (DOA). This assessment is valid only when no neuromuscular blocking agents have been administered as part of general anaesthesia and the patient therefore retains the physical capacity to respond. When such a drug is used, this ability is negated, regardless of the conscious level; it is then virtually impossible to differentiate an awake, paralysed patient from someone suitably anaesthetised using clinical signs of responsiveness alone. Furthermore, when a neuromuscular agent is used, indirect autonomic responses (such as tachycardia, elevated blood pressure or lacrimation) also become unreliable as signs of consciousness (NICE 2012). Therefore, a reliable method of DOA measurement is keenly sought.

The word "anaesthesia" is derived from a Greek term meaning "without sensation". It is a controlled, temporary state of loss of sensation and awareness that is induced for medical purposes. General anaesthesia is a controlled, reversible state of unconsciousness achieved by the administration of drugs, providing haemodynamic stability and the prevention of awareness, pain, recall, distress and movement in patients during surgery. It represents a balanced status between the amount of anaesthetic agent administered and the conscious level of the patient.

While accidental awareness under general anaesthesia (AAGA) can certainly be prevented by administering large doses of drugs, this will produce excessive DOA with consequent adverse effects such as haemodynamic instability, postoperative nausea and vomiting, cognitive dysfunction and prolonged length of stay in the post-anaesthesia recovery unit (PACU). Persistent intra-operative hypotension is perhaps the most important consequence as it carries the risk of end-organ damage, especially amongst high-risk patients or those with pre-existing comorbidities. Although the anaesthetist may be able to attenuate these risks by decreasing the anaesthetic dose or administering vaso-active agents, being able to measure the DOA has the potential to inform accurate dosage of both classes of drug, mitigating the risks of both awareness and cardiovascular instability. It is impossible to generalise the clinical effects of all the agents used in anaesthesia as there exists enormous variability according to the age, weight and physiological reserve of the individual (Rani and Harsoor 2012).

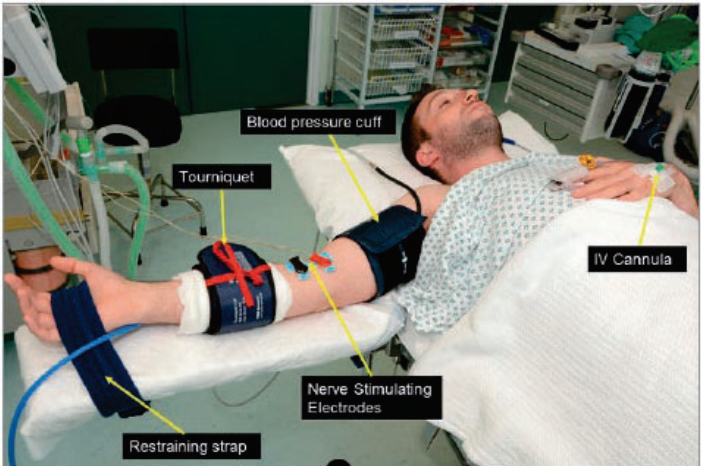

Fig. 9-1. Isolated forearm technique. Reproduced with permission (Report and findings of the 5th National Audit Project [NAP5]).

One of the early clinical DOA methods, no longer widely used outside a research setting, was the isolated forearm technique (Figure 9-1). In this technique, the patient's forearm is "isolated" from the systemic circulation by the inflation of a tourniquet on the forearm to a value above the systolic blood pressure. This is performed after induction of anaesthesia, but prior to the administration of neuromuscular blocking agents (NMBAs), so that

the latter drugs do not reach the isolated arm. In the event of intra-operative awareness, the patient would be able to move the isolated, non-paralysed arm, either spontaneously or on command (Tunstall 1977). Concurrent peripheral nerve stimulator monitoring on the ipsilateral arm ensures its continued isolation from the systemic NMBA. A major limitation is that the method is only possible for a short period of time before tourniquet-induced tissue ischaemia itself impairs muscle contractions. Although intuitively, a response to command during an anaesthetic might be considered a sign of awareness and therefore indicative of too light a plane of anaesthesia, multiple studies (Sebel et al. 2004) (Sandin et al. 2000) (Avidan et al. 2008) have shown that while movement may occur intra-operatively, this is not necessarily accompanied by postoperative recall.

A second, also mainly historical, DOA technique is that of lower oesophageal sphincter contractility (Evans, Davies, and Wise 1984). The method relies on the non-striated muscles of the lower oesophageal sphincter retaining their contractility even after the administration of NMBAs. Two types of smooth muscle contractions – spontaneous and evoked by the inflation of a balloon on a catheter – can be measured by an endoscopic pressure transducer. During general anaesthesia the frequency, latency and amplitude of both types of muscular contractions are significantly reduced, rising again as consciousness is regained. An exact threshold has not been described, thereby limiting the clinical application of this method.

Modern DOA monitors

Researchers have looked for decades for an accurate way to monitor the level of consciousness of patients undergoing general anaesthesia. Many employ different data points derived from the electrical activity of the brain. Ideally the chosen variables should have a range of values that are distinct in the conscious and unconscious state and do not overlap. It is also desirable for the sensitivity of the monitoring system, and therefore the value presented to the clinician, to be independent of both the anaesthetic agent used and the physiology of the individual (Bruhn et al. 2006).

Several techniques have been developed and implemented over the years (Shepherd et al. 2013), and DOA monitors generally operate on one of two principles:

1. Spontaneous electro-encephalography (EEG)
2. Evoked EEG in the form of auditory evoked potentials (AEP).

EEG

Caton first described the EEG in 1875 by detecting currents through the skulls of canines and primates using a galvanometer and electrodes (Haas 2003). This work was subsequently extended to humans, and a decade later the effects of morphine and barbiturates on the EEG waveform were described (Hajat, Ahmad, and Andrzejowski 2017).

In the present day, the EEG signal is acquired through gel electrodes. Signals are digitised, amplified and filtered to isolate the desired waveform from other biological potentials arising from electrocardiographic, electromyographic or ocular activity, as well as external artefact such as mains power interference.

The EEG waveform is the sum of many individual sine waves, the frequencies of which vary up to approximately 50 Hz (Davey and Diba 2011). These are grouped into frequency bands (Table 9-1).

Table 9-1. EEG waveform band names and corresponding frequencies. Reproduced with permission (Davey and Diba, Ward's Anaesthetic Equipment, Elsevier publishing).

Band	**Frequency range (Hz)**	**Conscious state**
Alpha	8-13	Awake, calm, deeply relaxed (eyes closed)
Beta	13-30	Alert and awake
Theta	4-8	Light sleep, REM sleep
Delta	<4	Deep sleep, unconscious, anaesthetised
Burst-suppression	No waves, isoelectric	Cortical silence, very deeply anaesthetised

"Raw" or unprocessed EEG (Figure 9-2) has limited use in the measurement of DOA as the majority of clinicians do not have the skillset to interpret this complex data in order to titrate the anaesthetic, particularly in real time whilst tending to the multiple other aspects of conducting anaesthesia.

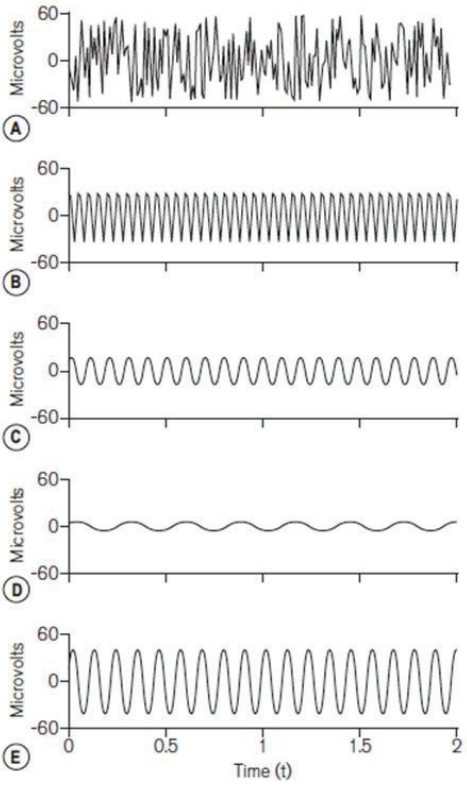

Fig. 9-2. A two-second epoch from an unprocessed EEG, demonstrating the constituent sine waves. A: Combined EEG waveform. B: 30 µV, 60° and 20 Hz. C: 15 µV, 30° and 10 Hz. D: 4 µV, 15° and 4 Hz. E: 40 µV 25° and 9 Hz. Reproduced with permission (Davey and Diba, Ward's Anaesthetic Equipment, Elsevier publishing).

In order for processing to occur, the EEG must be converted from a smooth continuous analogue signal into a digital one. Converting raw EEG signals into a single figure is heavily reliant on the quality of the signal at the time of recording. After processing, the EEG is then subjected to what are known as time-domain and frequency-domain analyses.

The most widely-used example of the time-domain analysis is the calculation of a burst-suppression ratio (BSR). To arrive at this, EEG activity not exceeding 5.0 mV and not lasting longer than 0.5 seconds is identified and considered as a fraction of total time. Burst-suppression of the EEG can be seen during very deep planes of anaesthesia, in the presence of traumatic brain injury or hypoxia, or when the basal metabolic rate of the brain is reduced, for example during deep hypothermia.

EEG consists of different, interrelated frequencies, and analysis of the signal is based on both the individual frequency and the relationship of the sine waves to each other. These relationships, known as phase coupling, correspond to the effect of anaesthetic agents on the EEG. As DOA increases, these changes become more apparent. This dose-response relationship is seen with both intravenous and inhalational agents. The most common application of processed EEG is as a DOA monitor in the peri-operative setting.

The last thirty years have shown a rapid advance in computer sciences and their application in healthcare. The possibility of miniaturisation of different components such as microprocessors which can analyse EEG waveforms and muscular activity have allowed the development of processed electromagnetic modalities such as bispectral index (BIS; Aspect Medical System, Newton MA, USA) and Spectral Entropy (GE Healthcare, Finland) (Bonhomme and Hans 2004). The number of trials reporting validation of these devices has risen significantly in the last decade, with BIS being the most extensively studied.

BIS

BIS is an EEG-derived variable that is calculated and displayed by a variety of devices and modules produced by several manufacturers. An example of the physical setup of this monitoring can be seen in Figure 9-3.

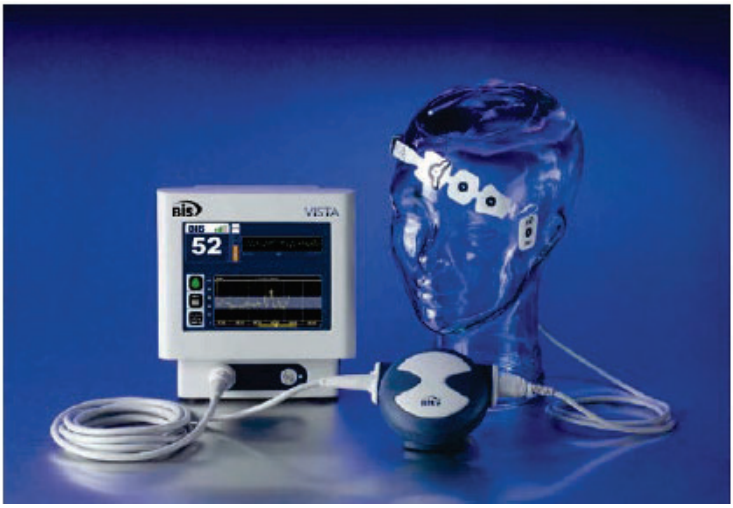

Fig. 9-3. BIS QUATRO monitor and monitoring strip. Reproduced with permission (Davey and Diba, Ward's Anaesthetic Equipment, Elsevier publishing).

BIS is calculated from the EEG using an algorithm which combines data both from bispectral analysis and more traditional methods. The overall product of the BIS algorithm is a dimensionless number on a scale from 1 to 100, which indicates the likelihood of consciousness. During general anaesthesia, a BIS value of less than 60 is indicative of reduced ability to recall, and values of 40-60 are commonly targeted. It is useful to note the patient's baseline BIS value prior to the administration of any drugs, as this may be reduced for a variety of reasons, particularly in the elderly, comorbid or acutely unwell patient. Application prior to induction of anaesthesia also helps to confirm the signal quality index (SQI), which should additionally be monitored throughout surgery to ensure that the BIS readings may be relied upon. SQI gives an indication of the reliability of the signal and is analysed over the preceding minute. This value is subject to interference from patient movement and surgical diathermy; it is most accurate in patients who are paralysed. Single-use BIS electrode strips are programmed with a unique alphanumerical code which can be noted on the anaesthetic chart for future interrogation of the module, should detailed values be required retrospectively (for example, where cases of AAGA are discovered postoperatively, or in medicolegal cases). An example of the BIS screen display may be seen in Figure 9-4.

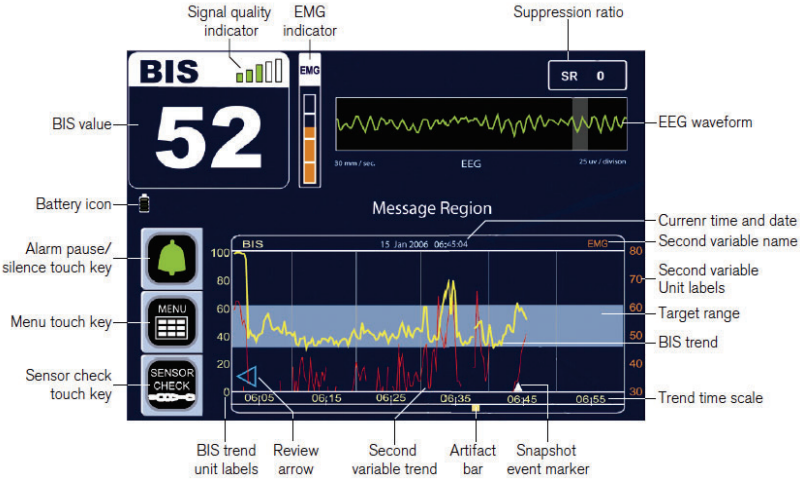

Fig. 9-4. BIS VISTA monitor. Reproduced with permission (Davey and Diba, Ward's Anaesthetic Equipment, Elsevier publishing).

The development of the BIS algorithm, and of bispectral index monitoring in general, has been described in several reviews (Johansen 2006) (Kearse et al. 1994). In 1992 the first algorithm, known as BIS 1.0, was released (Gounon 2018), having been developed using raw EEG data obtained from young, fit patients undergoing general anaesthesia. The EEG features that best predicted movement on incision were identified and combined in an index which was then tested prospectively (Davey and Diba 2011). In the 1990s, research demonstrated that the neural signals arising due to incision-induced movement were distinct from those associated with hypnosis. As a result, a second algorithm, 2.0, was formulated to predict the latter. The third and subsequent iterations attempted to improve BIS performance at extremes of anaesthetic depth and to mitigate artefactual error.

The latest "VISTA" generation of BIS monitors feature the 4.0 or 4.1 version of the algorithm. In these versions BIS is calculated using data from sensors containing four rather than three electrodes, with the fourth electrode placed above and lateral to the eyebrow.

BIS is validated against postoperative recall rather than intra-operative ability to obey commands. It is thus perhaps better described as a "recall probability" monitor, and not an "awareness" monitor. The UK National Institute for Health and Care Excellence (NICE) guidance shares this

opinion (NICE 2012), noting that "the output from these monitors reflects the probability of (un)consciousness in a given patient". The authors of this guideline also state that a BIS (or E-entropy) output reading of 40–60 indicates a low probability of awareness, but there is no clarification as to what "low" means. Similarly, the nature of the relationship between level of awareness and changing output reading is unsettlingly opaque.

If using BIS to assess DOA, one has to be reassured that it is adequate for any imminent change in the surgical stimulus. BIS can be as low as 30 during normal sleep (Sleigh et al. 1999), but the state of natural sleep is clearly not appropriate to allow surgery. The value given by BIS encompasses several different biological brain states and is not specific to general anaesthesia. Therefore, a BIS value of 50 immediately before a major stimulus such as skin incision or airway manipulation is likely to be inadequate. Painful stimuli release catecholamines and usually result in an increase in BIS. In an obstetric study employing the isolated forearm technique, it was calculated that a BIS as low as 27 was required to abolish forearm response at laryngoscopy (Zand et al. 2014).

A fascinating study was performed by a group in Australia, who showed that volunteers exposed to NMBAs alone demonstrated a drop in BIS to values signifying general anaesthesia, whilst still retaining consciousness (as demonstrated via the isolated forearm technique). The investigators concluded that BIS may therefore be an unreliable predictor of AAGA in patients who have received NMBAs, due to the contribution of EMG to the overall BIS value (Schuller et al. 2015). This may also be seen in normal anaesthetic practice when a bolus of NMBA is given to a patient intra-operatively.

Entropy

The E-Entropy module was designed in the early 2000s by Datex-Ohmeda and used as a depth of anaesthesia module for their S/5 anaesthesia monitor. It is based on the concept of "entropy", meaning the assessment of the degree of disordered signal within the spontaneous EEG.

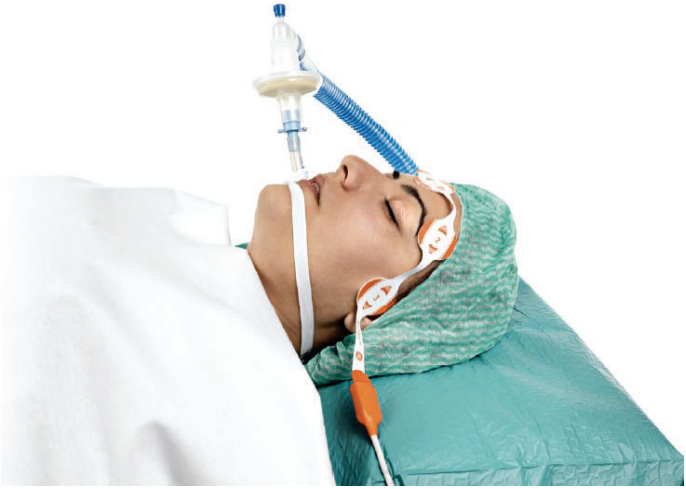

Fig. 9-5. E-Entropy monitoring strip. Reproduced with permission (www3.gehealthcare.co.uk/~/media/downloads/uk/product/anaesthesia/).

If the awake EEG is characterised by what could be termed a chaotic signal, then decreasing levels of consciousness are associated with a more uniform signal as the number of signal generators diminishes and slower-wave activity becomes more dominant. Therefore, by determining the proportion of disorder, or entropy, within the power spectrum of the EEG, it is suggested that anaesthetic depth may be objectively estimated. In contrast to the algorithms used by BIS, E-Entropy uses a relatively simple mathematical calculation with the resultant numerical scale deliberately manipulated to correlate with the BIS values now familiar to many anaesthetists. A three-electrode sensor (Figure 9-5), similar in appearance and application to that for BIS, is used to acquire a single-channel EEG. From this, the module calculates two values: one between 0 and 91 for "state entropy" (SE), which reflects cortical activity over the frequency range 0.8–32 Hz; and a second value between 0 and 100 for "response entropy" (RE) over the frequency range 0.8–47 Hz (Figure 9-6). The latter incorporates components of the frontalis muscle EMG. The manufacturers recommend that both values should, similarly to BIS, be kept between 40 and 60 during surgery under general anaesthesia. RE becomes equal to SE when the EMG power is zero, otherwise it is always the higher value; rapid rises in RE, or where RE exceeds SE by more than 5-10 units, are situations said to reflect relative analgesic inadequacy. This is because it is hypothesised that, in the case of deficient analgesia in a non-paralysed

patient, facial EMG activity increases before any change in the EEG, leading to an increase in RE before any change in SE. Where SE is above 60, a higher anaesthetic dose is required, as with BIS. E-Entropy also calculates a burst-suppression ratio, which should be 0% during general anaesthesia; higher values, such as that seen in Figure 9-6, often correlate with an unnecessarily deep plane of anaesthesia, typically accompanied by low RE and SE values as shown.

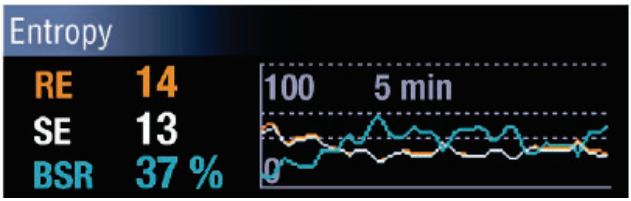

Fig. 9-6. The E-Entropy monitor displays two numbers: state entropy (SE) and response entropy (RE), with higher frequency EMG activity being included in the latter. Reproduced with permission (www.clinicalview.gehealthcare.com).

Both E-Entropy and BIS values rise in the presence of a noxious stimulus, but the rate of increase is not always the same; RE may respond to noxious stimuli faster. In a head-to-head study of BIS and E-Entropy, the RE and SE values prior to skin incision were found to be significantly lower in patients who did not move when compared to those who those who did; however, BIS remained unchanged. All EEG variables increased significantly with rising intensity of electrical stimulation (Takamatsu, Ozaki, and Kazama 2006).

In general, E-Entropy appears to perform no better than BIS in terms of correlation with effect site drug concentration and prediction of clinical endpoints (Takamatsu, Ozaki, and Kazama 2006). In sedated patients (as opposed to fully anaesthetised), the frontalis EMG renders interpretation of SE and RE values difficult and so BIS might be of greater utility in this scenario.

Narcotrend

Narcotrend™ (software version 4.0; MonitorTechnik, Bad Bramstedt, Germany) was released in 2001 and was designed for use both clinically in operating theatres and intensive care units, and also for clinical research. The Narcotrend-Compact M includes the Narcotrend-Index, a processed

EEG monitor which may be used as an aid in monitoring the effects of certain hypnotic anaesthetic agents.

Fig. 9-7. Narcotrend monitor and display. Reproduced with permission (www.narcotrend.de/deutsch/eeg-monitoring.html).

In Narcotrend (Figure 9-7), the EEG is acquired from one reference and two recording electrodes positioned on the forehead. Artefacts are rejected, and the data are analysed using an algorithm which assigns a Narcotrend "stage". There are six stages, A (conscious) to F (deep general anaesthesia with increasing burst-suppression). A recent version also includes a numerical index between 0 and 100, similar to that popularised by BIS, with lower values indicating deep hypnosis and higher ones increasing wakefulness.

The algorithm is however distinct from that of BIS in that it was developed purely as a means for objective analysis of the EEG waveform, using time- and frequency-domain information. No clinical correlates were involved (Kreuer and Wilhelm 2006).

Danmeter

Auditory evoked potentials (AEPs) attracted interest in the 1980s due to their clear dose-response relationship with anaesthetic agents (Bruhn et al. 2006).

When general anaesthesia is induced, a reproducible pattern of events occurs in the cerebral cortex in response to any auditory stimulus. The early cortical response occurs 10-100 ms after the initial stimulus and it is termed the mid-latency auditory evoked potential (MLAEP). MLAEP waves are generated in the medial geniculate and primary auditory cortex. Anaesthesia increases the latency and decreases the amplitude of MLAEP waves.

The A-Line AEP monitor/2 (AEP Monitor/2, Danmeter A/S, Odense, Denmark) is a hybrid spontaneous EEG and AEP monitor (Davey and Diba 2011). For the AEP component, 65–70 dB click stimuli are administered at 9 Hz through headphones, the response being recorded with scalp electrodes. A "click detection" function alerts the clinician if the auditory stimulus ceases for any reason. The response signal undergoes pre-processing, during which artefact is rejected and band-pass filtering applied. Subsequent extraction of the AEP from background cortical activity takes time and results in some latency. In current versions of the monitor, the replacement of "moving time averaging" with an autoregressive model using a proprietary mathematical method called ARX modelling has reduced the update lag time from 35 to 6 seconds.

SedLine and Root® (Masimo) brain function monitor

The addition of cerebral perfusion monitoring to EEG allows for greater correlation between brain function and cerebral blood flow. The SedLine and Root (Masimo) brain function monitor (SedLine® and Root® Masimo, USA) (Figure 9-8) utilises bilateral sensor strips and displays a processed EEG presented as Patient State Index (PSi™), a proprietary calculated measure of brain activity that reflects the patient's current level of hypnosis. PSi features enhanced filtering of higher frequency EMG signal, and so is said to be less influenced by this particular source of artefact.

Fig. 9-8. SedLine Masimo brain function monitor. Reproduced with permission (www.masimo.com/products/continuous/root/root-sedline/).

Evidence base and guidelines

Over the last 15 years there have been several large multi-centre trials studying the utility of DOA, with varying results. The majority of these have looked at BIS and so this technique has the largest volume of supporting evidence to date. The metric of interest in the majority of studies has been the incidence of AAGA. Knowledge of the background incidence of AAGA stems from two important pieces of work from the US and UK respectively: the Incidence of Awareness during Anaesthesia trial (Sebel et al. 2004), which reported 1-2 cases per thousand patients; and the 2013 5th National Audit Project (Pandit, Cook, Jonker, O'Sullivan, et al. 2013), which demonstrated a much lower overall incidence of approximately 1 in 19,000 anaesthetics. The single-centre SAFE-1 study (Sandin et al. 2000) interviewed patients at three distinct time points after general anaesthesia: immediately on waking in the PACU, then at 1-3 days and 7-14 days postoperatively. The incidence of awareness detected by these means was 0.18% amongst patients who received NMBAs, and 0.10% in those who did not.

Notable trials in favour of the use of DOA monitoring – specifically BIS – include the B-aware trial (Myles et al. 2004). This was a prospective,

international, multi-centre, randomised control trial that recruited patients requiring general anaesthesia with NMBAs for a variety of operations known to confer higher risk for AAGA, including Caesarean section, cardiac and trauma surgery. An incidence of 0.9% was seen in the in routine care group versus 0.2% in the BIS group, and the authors concluded that the use of BIS reduced the incidence of awareness with recall in this high-risk cohort by approximately 82%. Conversely, the subsequent and similarly-designed B-unaware trial, which focused on patients requiring cardiac surgery, failed to detect a reduction in awareness in patients receiving BIS monitoring (Kertai et al. 2010).

Few studies have attempted to correlate BIS and end tidal anaesthetic agent (EtAA); Avidan et al (Avidan et al. 2008) concluded that there was no reduction in AAGA incidence with versus without BIS monitoring, and also that the addition of BIS did not help anaesthetists administer lower concentrations of volatile agent.

The evidence is therefore conflicting and prevents BIS from being used routinely in addition to EtAA for patients receiving conventional inhalational anaesthesia. There are no convincing data to support a BIS value of 40-60 over a minimum alveolar concentration (MAC) of at least 0.7 as a better predictor of AAGA risk. It is therefore patients who may not tolerate a MAC of 0.7 who stand to benefit the most from the addition of BIS to a volatile-based anaesthetic.

The aforementioned NICE guidance advises the use of a processed EEG DOA monitor (BIS, E-Entropy or Narcotrend) for patients deemed to be at high risk of either under- or over-dosage of anaesthesia, and in all patients in whom total intravenous anaesthesia (TIVA) is used (NICE 2012). Groups considered at high risk of inappropriately high or low anaesthetic dosing include: the elderly; those with unstable physiology; patients requiring rapid sequence induction; and women undergoing Caesarean section under general anaesthesia. The NAP5 recommendations were broadly in agreement (Pandit, Cook, Jonker, O'Sullivan, et al. 2013), adding that all patients receiving NMBAs in any setting should receive DOA monitoring.

The high-risk groups mentioned above are likely to add up to significantly more than the 2.8% of patients who received DOA monitoring as part of a general anaesthetic, as reported by the Activity Survey section of NAP5 (Pandit, Cook, Jonker, O'Sullivan, et al. 2013); in other words, DOA monitoring is significantly under-used in everyday anaesthetic practice

according to these criteria. In reality, the conflicting evidence base and financial pressures have likely contributed to the variable uptake of DOA monitoring and differing practice between anaesthetists, even within the same institution.

Limitations

Drugs

Different anaesthetic agents variously affect EEG-derived DOA readings, again with BIS being the most well understood.

Ketamine is used not only as an induction agent but more recently as a component of multimodal analgesia for both acute and chronic pain patients requiring surgery. As useful an adjunct as this drug is, it also increases cerebral metabolic rate and leads to a rise in theta activity, influencing the way in which BIS values are calculated by the algorithm. This unfortunately renders subsequent interpretation of BIS impossible. Similar effects are observed with both dexmedetomidine and xenon.

Opiates, especially at high dose, have a particular effect on the EEG but are also devoid of the ability to prevent recall; their precise relationship with BIS is not yet fully understood (Hajat, Ahmad, and Andrzejowski 2017). An opiate-based anaesthetic, such as one using a high-dose remifentanil infusion, shows little variation in BIS, with a blunted increase ("trend spikes") following a stimulating event (Zand et al. 2014).

Nitrous oxide does not produce any changes to BIS when used alone or when administered with propofol. However, when combined with sevoflurane there is a small additive effect (Harris et al. 2006).

When propofol is given in prolonged infusions, its accumulation can produce motor neurone suppression and reduction of motor evoked potential (MEP) responses. This will not only require increasing stimulating thresholds in order to elicit responses but may also trigger false alerts. This phenomenon of "anaesthetic fade" can be minimised by titrating the appropriate DOA.

Whatever combination of drugs is used, the individual effects on the processed EEG are not individually discernible.

Practicalities

There are multiple factors that may alter the accurate reading of BIS in the hypnotic state, including EMG activity, neuromuscular blockade, electrical interference, and patient-specific abnormal EEG patterns.

When DOA monitors are used in patients who are not paralysed or in those in whom the NMBA is wearing off, EMG artefact from the frontalis muscle can interfere with the interpretation of EEG signals, as previously mentioned. EMG activity can obfuscate the EEG signal, resulting in an artefactual increase in the value displayed by the DOA monitor.

Physiological factors such as hypotension, hypoxaemia, hypothermia and hypoglycaemia also can affect EEG-derived indices of DOA and have not been well explored in the literature.

Finally, BIS electrode strips can be difficult to apply in certain neurosurgical approaches, such as frontal craniotomy. In such circumstances the strip may be applied across the bridge of the nose, which has been demonstrated to adequately detect frontal lobe signals (Nelson et al. 2013).

Summary

At present, there is no ideal method of measuring DOA during general anaesthesia or sedation. There is also a paucity of head-to-head trials to support one EEG-based system over another. What is clear is that whilst most research has been directed towards the prevention of AAGA, DOA monitoring also enables anaesthetists to avoid unnecessarily high doses of anaesthetic and so is particularly suited to the acutely unwell, comorbid patient undergoing emergency surgery. Notably, BIS parameters appear to correlate with outcome: a “triple low” (reduced BIS, blood pressure and MAC) is associated with higher mortality (Sessler et al. 2012).

Current guidance is clear that patients receiving TIVA with NMBAs should receive DOA monitoring. Ideally this should also include transfers of sedated or anaesthetised patients. In reality, this is challenging and, in some cases, impossible with current technology (for example, during magnetic resonance imaging, which requires compatible equipment free of magnetic materials). It is also important to note that DOA monitors remain unvalidated in the critical care population, who are often most likely to require such transfers.

Finally, EEG-based DOA monitoring is but one tool in the arsenal of the anaesthetist, and the information it provides must be correlated with clinical data and interpreted in the context of the anaesthetic and surgical procedure at hand.

References

Avidan, M. S., L. Zhang, B. A. Burnside, K. J. Finkel, A. C. Searleman, J. A. Selvidge, L. Saager, M. S. Turner, S. Rao, M. Bottros, C. Hantler, E. Jacobsohn, and A. S. Evers. 2008. "Anesthesia awareness and the bispectral index." *New England Journal of Medicine* 358 (11):1097-108.

Bonhomme, V., and P. Hans. 2004. "Monitoring depth of anaesthesia: is it worth the effort?" *European Journal of Anaesthesiology* 21 (6):423-8.

Bruhn, J., P. S. Myles, R. Sneyd, and M. M. Struys. 2006. "Depth of anaesthesia monitoring: what's available, what's validated and what's next?" *British Journal of Anaesthesia* 97 (1):85-94.

Davey, A., and A. Diba. 2011. *Ward's Anaesthetic Equipment*. Edited by A. Davey and A. Diba. 6th Edition ed, *Ward's Anaesthetic Equipment*. London: Saunders.

Evans, J. M., W. L. Davies, and C. C. Wise. 1984. "Lower oesophageal contractility: a new monitor of anaesthesia." *Lancet* 1 (8387):1151-4.

Gounon, L, J. 2018. "Monitoring depth of anaesthesia, a longstanding enterprise " *The History of Anaesthesia Society Proceedings* 51:70-72.

Haas, L. F. 2003. "Hans Berger (1873-1941), Richard Caton (1842-1926), and electroencephalography." *Journal of Neurology, Neurosurgery & Psychiatry* 74 (1):9.

Hajat, Z., N. Ahmad, and J. Andrzejowski. 2017. "The role and limitations of EEG-based depth of anaesthesia monitoring in theatres and intensive care." *Anaesthesia* 72 Suppl 1:38-47.

Harris, R. S., O. Lazar, J. W. Johansen, and P. S. Sebel. 2006. "Interaction of propofol and sevoflurane on loss of consciousness and movement to skin incision during general anesthesia." *Anesthesiology* 104 (6):1170-5.

Johansen, J. W. 2006. "Update on bispectral index monitoring." *Best Practice & Research. Clinical Anaesthesiology* 20 (1):81-99.

Kearse, L. A., Jr., P. Manberg, F. DeBros, N. Chamoun, and V. Sinai. 1994. "Bispectral analysis of the electroencephalogram during induction of anesthesia may predict hemodynamic responses to laryngoscopy and intubation." *Electroencephalography & Clinical Neurophysiology* 90 (3):194-200.

Kertai, M. D., N. Pal, B. J. Palanca, N. Lin, S. A. Searleman, L. Zhang, B. A. Burnside, K. J. Finkel, M. S. Avidan, and B. Unaware Study Group. 2010. "Association of perioperative risk factors and cumulative duration of low bispectral index with intermediate-term mortality after cardiac surgery in the B-Unaware Trial." *Anesthesiology* 112 (5):1116-27.

Kreuer, S., and W. Wilhelm. 2006. "The Narcotrend monitor." *Best Practice & Research. Clinical Anaesthesiology* 20 (1):111-9.

Myles, P. S., K. Leslie, J. McNeil, A. Forbes, and M. T. Chan. 2004. "Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial." *Lancet* 363 (9423):1757-63.

Nelson, P., J. A. Nelson, A. J. Chen, and W. A. Kofke. 2013. "An alternative position for the BIS-Vista montage in frontal approach neurosurgical cases." *Journal of Neurosurgical Anesthesiology* 25 (2):135-42.

NICE. 2012. Depth of anaesthesia monitors – Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M. In *DG6*. London: National Institute for Health and Care Excellence.

Pandit, J. J., T. M. Cook, W. R. Jonker, E. O'Sullivan, and Anaesthetists of the Association of Anaesthetists of Great Britain National Audit Project of the Royal College of, Ireland. 2013. "A national survey of anaesthetists (NAP5 baseline) to estimate an annual incidence of accidental awareness during general anaesthesia in the UK." *British Journal of Anaesthesia* 110 (4):501-9.

Pandit, J. J., T. M. Cook, W. R. Jonker, E. O'Sullivan, Anaesthetists the Association of Anaesthetists of Great National Audit Project of the Royal College of, Britain, and Ireland. 2013. "A national survey of anaesthetists (NAP5 Baseline) to estimate an annual incidence of accidental awareness during general anaesthesia in the UK." *Anaesthesia* 68 (4):343-53.

Rani, D. D., and S. Harsoor. 2012. "Depth of general anaesthesia monitors." *Indian Journal of Anaesthesia* 56 (5):437-41.

Sandin, R. H., G. Enlund, P. Samuelsson, and C. Lennmarken. 2000. "Awareness during anaesthesia: a prospective case study." *Lancet* 355 (9205):707-11.

Schuller, P. J., S. Newell, P. A. Strickland, and J. J. Barry. 2015. "Response of bispectral index to neuromuscular block in awake volunteers." *British Journal of Anaesthesia* 115 Suppl 1:i95-i103.

Sebel, P. S., T. A. Bowdle, M. M. Ghoneim, I. J. Rampil, R. E. Padilla, T. J. Gan, and K. B. Domino. 2004. "The incidence of awareness during

anesthesia: a multicenter United States study." *Anesthesia & Analgesia* 99 (3):833-9, table of contents.

Sessler, D. I., J. C. Sigl, S. D. Kelley, N. G. Chamoun, P. J. Manberg, L. Saager, A. Kurz, and S. Greenwald. 2012. "Hospital stay and mortality are increased in patients having a "triple low" of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia." *Anesthesiology* 116 (6):1195-203.

Shepherd, J., J. Jones, G. Frampton, J. Bryant, L. Baxter, and K. Cooper. 2013. "Clinical effectiveness and cost-effectiveness of depth of anaesthesia monitoring (E-Entropy, Bispectral Index and Narcotrend): a systematic review and economic evaluation." *Health Technology Assessment (Winchester, England)* 17 (34):1-264.

Sleigh, J. W., J. Andrzejowski, A. Steyn-Ross, and M. Steyn-Ross. 1999. "The bispectral index: a measure of depth of sleep?" *Anesthesia & Analgesia* 88 (3):659-61.

Takamatsu, I., M. Ozaki, and T. Kazama. 2006. "Entropy indices vs the bispectral index for estimating nociception during sevoflurane anaesthesia." *British Journal of Anaesthesia* 96 (5):620-6.

Tunstall, M. E. 1977. "Detecting wakefulness during general anaesthesia for caesarean section." *British Medical Journal* 1 (6072):1321.

Zand, F., S. M. Hadavi, A. Chohedri, and P. Sabetian. 2014. "Survey on the adequacy of depth of anaesthesia with bispectral index and isolated forearm technique in elective Caesarean section under general anaesthesia with sevoflurane." *British Journal of Anaesthesia* 112 (5):871-8.

CHAPTER 10

GETTING IONM RIGHT IN CHILDREN

NATASHA WOODMAN
JAMES GILL

Introduction

This chapter aims to highlight the key differences and considerations for a paediatric patient – as compared to an adult – requiring intra-operative neuromonitoring (IONM). These differences are particularly evident below the age of two years. Children have a smaller body surface area available for the application of electrodes, which may not only limit their number but also necessitate closer proximity to the surgical field, leading to interference and difficult interpretation of recordings. IONM electrodes may also restrict concurrent placement of depth of anaesthesia (DOA) monitors, meaning that at times the anaesthetist must instead adapt by incorporating data from the unprocessed electro-encephalogram (EEG) or electrocorticograph (ECoG) into their clinical assessment of anaesthetic depth. In children the myelination of conduction pathways may not be fully mature, which further hinders interpretation of IONM; and, should an alert be raised, conventional "wake-up" testing is rarely a feasible option. Pharmacologically, total intravenous anaesthesia (TIVA) is less well established and studied in the paediatric population, and propofol infusion syndrome (PrIS) is a concern in this group, especially in lengthy procedures.

IONM techniques were developed to provide feedback on the integrity of vulnerable neural structures and thereby improve the safety of neurosurgical procedures. The advent of new intra-operative methodologies to assess specific neural pathways, such as the corticospinal tracts, dorsal columns, and nerve roots, has made IONM standard practice in many paediatric and adult institutions.

Paediatric procedures using IONM

Brain tumours

Around half of paediatric brain tumours are glioma subtypes, with astrocytoma accounting for 45% (Wilne et al. 2013). These tumours may be pilocytic astrocytomas arising in the cerebellum, or diffuse midline gliomas of the brainstem. Medulloblastomas, an embryonal tumour, are the second most common paediatric brain tumours (20%) and these too are found in the posterior fossa. Owing to the critical functions of the brainstem, the resection of tumours in this location frequently calls for IONM. The cranial nerve nuclei, reticular activating system and ascending and descending long tracts are vulnerable to damage, with potentially devastating consequences. Traditional landmark surgical techniques are unable to appreciate and compensate for the distortion and mass effect caused by such lesions. Photographs of a child prepared for cranial nerve IONM can be found in Figures 10-1 and 10-2.

Fig. 10-1. An anaesthetised child prepared for neurosurgery. Placement of IONM electrodes to monitor cranial nerves 3-12 can be seen, along with a soft gauze bite block. (Photograph by parental permission)

Fig. 10-2. The same child from Fig. 10-1, now positioned prone for surgery with head in pins and electrodes taped in place. (Photograph by parental permission)

Spinal surgery

Paediatric spinal surgery is performed for a multitude of pathologies, including congenital neural tube defects, space-occupying lesions, scoliosis correction and trauma. The most frequent indications for IONM are the correction of spinal deformities, including kyphoscoliosis and spondylolisthesis, intra- and extramedullary tumour resection, and spinal dysraphisms. Common IONM modalities used in such procedures include

somatosensory evoked potentials (SSEPs), motor evoked potentials (MEPs), electromyography (EMG), and EEG.

IONM modalities used in children

IONM encompasses mapping and monitoring techniques, both important in the paediatric setting. Mapping identifies functional nervous tissue, for example within a lipoma during untethering of the spinal cord, or distorted by a brainstem glioma; however, it only provides functional feedback for a specific moment in time. Monitoring would also be required in both these examples, in order to continuously assess the functional integrity of neural pathways as surgeons operate, detecting neurophysiological changes in near real time with the intention of avoiding inadvertent neurological damage.

Motor evoked potentials

Fulkerson and colleagues made the first report of reliable and safe MEP recording in ten children under the age of three years undergoing neurosurgical spinal procedures (Fulkerson et al. 2011). They observed a higher MEP threshold in this age group as compared to adults: the baseline threshold voltages were greater than 300 V in all subjects. Yang and colleagues recorded MEPs during scoliosis correction surgery in two groups of children under eleven years of age (Yang et al. 2012). Successful monitoring was seen in both children receiving a propofol TIVA-based anaesthetic and those given low dose (0.5-1 %) sevoflurane, supplemented with other agents. This is in line with the generally accepted minimum alveolar concentration (MAC) of up to 0.5 being compatible with IONM. Higher concentrations of halogenated anaesthetic agents increase the MEP stimulus threshold and block signals in a dose-dependent manner.

Children may have a raised threshold to elicit MEPs due to their developing motor system, where myelination of anatomical connections between the brain and spinal cord is still being established. However, this may be partially counterbalanced by their shorter limb length and thinner skulls, which offer a lower resistance to stimulation.

It is known that MEP responses degrade or “fade” over the duration of a procedure, despite unchanged anaesthetic and physiological conditions. It is also observed that the voltage threshold is often higher at the end of a case than at baseline, regardless of anaesthetic technique. The rate of rise

of voltage threshold has been demonstrated to be inversely proportional to anaesthetic duration (Lyon, Feiner, and Lieberman 2005) (Sala, Krzan, and Deletis 2002), and so progressively higher stimulating voltages are required to maintain responses. Recognition of anaesthetic fade is important when interpreting changes in MEP response to avoid false positive findings. This is especially important in myelopathic subjects, in which the effect is more pronounced (Lyon, Feiner, and Lieberman 2005) (Sala, Krzan, and Deletis 2002).

From a practical perspective, caution must be exercised in applying the corkscrew MEP electrodes to the delicate scalp of very young children or babies; the needles must also avoid open fontanelles and any cerebrospinal fluid diversion or shunt system already in situ.

Somatosensory evoked potentials

In this modality, peripheral sensory nerves are stimulated to test responses at the sensory cortex. Typically, the integrity of SSEPs running through the brainstem is monitored with a stimulus at the wrist to either the median or ulnar nerve; the response is monitored at the thalamocortical radiations to the primary sensory cortex (Sala, Coppola and Tramontano 2015). For pontine and midbrain masses, SSEPs do not have localising value, but do provide feedback on the general integrity of the brainstem; they are informative in the resection of tumours at the cervico-medullary level.

Unfortunately, there are several limitations associated with SSEPs that make concurrent use with MEPs imperative. SSEPs require 10-40 seconds to average results, creating a lag in surgical feedback; they may also be lost entirely during an early myelotomy in intramedullary spinal cord tumour surgery. It is speculated that in children under the age of approximately ten years, such congenital tumours displace the dorsal columns laterally, allowing SSEPs to be preserved after myelotomy. These disadvantages are summarised by Sala (Sala, Krzan and Deletis 2002).

Brainstem auditory evoked potentials

The role of BAEPs is largely confined to cerebellopontine angle surgery at present; in the paediatric setting, this most commonly involves the resection of acoustic neuromas in children with neurofibromatosis type 2. Transient acoustic stimuli are emitted from scalp or peripheral electrodes, and the electrical responses denoting auditory pathway function are recorded in the form of seven different waves by recording electrodes.

These detect changes in wave amplitude and latency. BAEPs are particularly sensitive to temperature change, and since the paediatric population are at greater risk of hypothermia than adults, it is important to use warmed fluids when irrigating the surgical field.

Electromyography

This technique observes the spontaneous activity of peripheral muscles in response to motor nerve impulses. However, it is neither sensitive nor specific, and is largely superseded by MEPs. Electrical silence could be the result of either motor nerve inactivity or complete transection. Equally, a degree of EMG activity consistent with nerve injury may also be inadvertently elicited by cold saline irrigation of the surgical field (Sala, Coppola and Tramontano 2015).

IONM alerts

The management of a change in evoked potentials is not specific to paediatric surgery and is discussed in more detail in other chapters. Typically, surgery is paused, and time allowed for recovery of the signals. Should surgical manipulation continue regardless, reversible injuries may progress to irreversible. The surgical field may be irrigated with warm saline to correct any hypothermia of the nervous tissue, and papaverine can be directly applied if perfusion is thought to be inadequate. An arterial cannula with beat-to-beat blood pressure monitoring is essential, allowing the anaesthetist to ensure normal or even supra-normal blood pressure at the point of any alert. For posterior fossa surgery, the transducer is best placed at the level of the external auditory meatus to correlate with cerebral perfusion. Serial arterial blood gas (ABG) sampling also allows monitoring for, and correction of, any anaemia limiting oxygen delivery to nervous tissue, thereby contributing to reduced signals. Multidisciplinary checklists are frequently employed to ensure all correctable factors are considered and optimised (Yu Wing-hay and Chung Chun-kwong 2019).

Some children with musculoskeletal deformities associated with the group of disorders known as mucopolysaccharidoses have developed neurological deficits after non-spinal surgery in the past. It has been demonstrated that IONM may be instrumental in preventing such adverse outcomes. Novel algorithms for guiding the peri-operative management of patients with mucopolysaccharidoses are useful tools for the provision of safe anaesthetic care in this high-risk cohort (Kandil et al. 2019).

A recent case review of paediatric patients undergoing coronal spinal deformity surgery found that IONM alerts with bilateral changes frequently responded to a combination of transfusion, increasing blood pressure, and surgical rod removal. Unilateral changes resulting from direct trauma, mainly during laminotomies, improved with removal of the cause. Following corrective actions in response to the alerts, all cases in the series were completed as planned. Signals returned to near baseline in the majority of patients at closure, with no new neurological deficits detected postoperatively. This demonstrated that safe correction of abnormal signals is possible with a systematic approach, and that signals did not necessarily have to recover to baseline values in order for the patient to be neurologically intact postoperatively (Lewis et al. 2019).

Anaesthetic technique

Pre-operative preparation

Pre-operative assessment should focus on the risks for peri-operative morbidity. The conscious level should be documented using an age-appropriate Glasgow Coma Scale (GCS). Examination of the cardiovascular system, including an echocardiogram of any murmurs detected clinically, is important in order to identify congenital cardiac septal defects; intracardiac shunting of an inadvertent venous air embolism (VAE) can be fatal. Other considerations include: pre-operative anticonvulsant therapy and its effect on neuromuscular blockade; hypovolaemia and deranged serum electrolytes due to vomiting associated with raised intracranial pressure (ICP); and ensuring a careful perinatal history, which may reveal intraventricular haemorrhage and other features associated with prematurity. Radiological investigations will provide details of the size and site of any lesion, the presence of hydrocephalus, and any cerebral pressure effects (Furay and Howell 2010).

In addition to the standard anaesthetic considerations, consent for anaesthesia with IONM should include the risk of accidental awareness, location of needle sites used for IONM, and the possibility of oral injury during airway manipulation or muscle stimulation. These risks will need to be discussed with the parent or carer and possibly the patient themselves depending on age and maturity. Premedication with midazolam may be considered if required, as benzodiazepines are generally compatible with IONM (Kandil et al. 2019).

General aspects of intra-operative management

Airway management in cases requiring IONM almost invariably involves tracheal intubation, and to facilitate this, a short-acting neuromuscular blocking agent (NMBA). NMBAs may be used at induction of anaesthesia, but not dosed repeatedly, in order to prevent interference with MEP and EMG monitoring. Alternatively, it may be possible to intubate the child without use of a NMBA, given sufficient depth of anaesthesia. Sugammadex may have a role if intubation required muscle relaxation and IONM was required very shortly afterwards; rocuronium or vecuronium would therefore be the NMBAs of choice.

Sizing of the tracheal tube may be affected by IONM requiring specialised tracheal tubes (for example, for vocal cord monitoring in thyroid surgery), and the neurophysiologist may require assistance in visualising the oropharynx for intra-oral probe placement. A soft bite block should be inserted prior to IONM to prevent intra-oral injury secondary to jaw muscle twitches. Appropriate temperature control of the operating theatre and patient should be ensured, especially for prolonged procedures. Ensure careful padding and protection to mitigate the risk of pressure injuries.

The impact of inhalational agents versus propofol on signal attainment is discussed in other chapters in this book. Halogenated anaesthetics and nitrous oxide do interfere with IONM reliability, but in the paediatric setting are often required at least at the start of a case for inhalational induction of anaesthesia, particularly for younger children. Volatile agents also have a propofol-sparing role and may reduce the risk of propofol infusion syndrome.

In spinal surgery, ketamine is often used as an adjunct to counter postoperative pain, which can be significant in scoliosis correction. Ketamine increases SEP and MEP amplitudes, and has proven useful in cases that would otherwise be unsuitable for monitoring because of low-amplitude, poorly defined MEP responses. Alpha-2 adrenergic agonists such as clonidine and dexmedetomidine should be used with caution whenever motor pathways are being monitored, as their administration can depress MEPs significantly. Intrathecal (IT) opioids are another adjunct used in some centres and evidence suggests that these do not significantly effect either SSEPs or MEPs (Levin, Strantzas, and Steinberg 2019).

Total intravenous anaesthesia

Optimal propofol TIVA requires a knowledge of pharmacokinetic-pharmacodynamic (PK-PD) profiles to predict both changes in blood concentrations (pharmacokinetics) and clinical effect (pharmacodynamics). Childhood is a period of multiple physiologic maturations, including variations in body composition regarding fluid, muscle, and fat proportions, and altered metabolic capacity. This means that the volumes of distribution and clearance rates of drugs change markedly with age. To add to the complexity, considerable inter-individual variability of the PK-PD profile exists within the paediatric population (Rigouzzo, Servin, and Constant 2010). These factors render mathematical modelling of drug behaviour less certain compared to adults, which goes some way to explaining the poor predictability of many of the published models.

There are two validated paediatric target-controlled infusion (TCI) programmes for propofol: Kataria (Kataria et al. 1994) and Paedfusor (Constant and Rigouzzo 2010) (Absalom et al. 2005). Kataria caters for children 3-16 years of age weighing 15-61 kg, whilst Paedfusor is broader: 1-16 years of age and 5-61 kg. At weights above 61 kg, children may be managed with the adult Marsh model. Nimmo et al have recently authored TIVA guidelines on behalf of the Association of Anaesthetists and Society for Intravenous Anaesthesia (Nimmo et al. 2018).

Depth of anaesthesia monitoring

EEG is an imperfect DOA monitor as it represents mainly cortical electrical activity, whereas anaesthesia impacts upon both cortical and subcortical structures. Processed EEG-based monitors such as Bispectral Index (BIS; Covidien, Boulder, USA), spectral entropy (E-Entropy; GE Healthcare, UK) and Narcotrend (Schiller, Switzerland) have been evaluated in children. Of these, BIS is the best studied; its founding data were derived from adult subjects, but BIS values correlate with clinical sedation scores in children aged 1-12 years, and modelled effect site concentration of propofol and opiates in children aged 1-16 years (Sadhasivam et al. 2006).

Another processed EEG monitor sometimes used in the paediatric population is the SedLine monitor (Masimo, USA), which uses a proprietary algorithm to produce a value known as the patient state index (PSI) (Schneider et al. 2003) (Drover and Ortega 2006). This algorithm incorporates EEG power, frequency and phase information from anterior-posterior

relationships of the brain, as well as coherence between bilateral brain regions. SedLine is considered most useful for monitoring patients undergoing propofol sedation (Lee et al. 2015).

The most uncertainty with this type of monitoring lies in the infant population, in whom the EEG is very different compared even to that of an older child. In this scenario the working relationship between the anaesthetist and neurophysiologist becomes even more important.

Peri-operative complications

Research and data are limited for management of the complications mentioned below. Principles are similar across adult and paediatric practice.

Brainstem dysfunction

Posterior fossa surgery brings a risk of brainstem compression, traction or stimulation, which can lead to sudden, extreme physiological changes that can be life-threatening. Though not related directly to IONM, this complication should be mentioned in a chapter concerning paediatric patients, in whom the majority of brain tumours arise in the posterior fossa. Surgery must be immediately paused before anaesthetic interventions are applied; these include ensuring adequate oxygenation, normocapnia and adequate depth of anaesthesia. Drugs for specific circumstances, such as magnesium for arrhythmias, esmolol for severe tachycardia, atropine for extreme bradycardia and vasoactive drugs for hypo- or hypertension should be readily available.

Drug extravasation

Extravasation of intravenous fluids or drugs not only risks intra-operative awareness but may also cause tissue necrosis. Referral for specialist management, often by a plastic surgeon, should be considered. Conservative management is often adequate but more serious injuries may require delayed debridement, possibly with split skin grafting if the area of skin loss is extensive. Prevention of these injuries remains the aim, through cannula site vigilance and appropriate setting of infusion device pressure alarms.

Propofol infusion syndrome

PrIS was first described by Parke (Parke et al. 1992) and given its current moniker by Bray (Bray 1998). In the latter's retrospective review of 18 children, progressive bradycardia eventually leading to asystole was seen with propofol infusions exceeding 4 mg/kg/h administered for 48 hours or longer. Cardiovascular dysfunction was frequently accompanied by a constellation of lipidaemia, fatty infiltration and enlargement of the liver, metabolic acidosis and skeletal muscle breakdown. Vasile and colleagues reviewed a larger series focusing on adult cases, identifying that catecholamines and corticosteroids are triggering agents for PrIS, and that patients with acute neurological or inflammatory illnesses are at particular risk (Vasile et al. 2003). The current mainstay of sedation on paediatric intensive care units is often a combination of an opiate and a benzodiazepine for this reason. Propofol TIVA is still used frequently and appropriately for paediatric patients, but clinicians should be mindful of total cumulative doses of propofol, particularly when a child may be undergoing repeated episodes of anaesthesia within a short period to facilitate their investigations and surgical management. The additional use of volatile agents is propofol-sparing and can mitigate this risk.

Propofol is known to depress mitochondrial function, and it should therefore be avoided altogether in patients with known or suspected mitochondrial disease. One case of PrIS occurred within just three hours in a 16-year-old patient with neonatal progeroid syndrome who was scheduled for correction of neuromuscular scoliosis, although the dose of propofol given was particularly high (Hermanns et al. 2006).

Therefore, during a long procedure with a propofol-based anaesthetic, patients should be monitored for arrhythmias, metabolic acidosis and a rising serum lactate. Adjunct investigations such as creatine kinase, troponin I, myoglobin, liver and renal function may also be informative.

Summary

Many types of paediatric neurosurgery benefit from the addition of IONM, most notably, posterior fossa tumour resections and scoliosis correction. An understanding of the differences in IONM compared to the adult population allows meaningful interpretation of signals. Children, especially with metabolic conditions, are at risk of PrIS as a consequence of propofol TIVA and this requires thoughtful mitigation. Processed EEG DOA monitoring is more limited in the paediatric population due to a

combination of EEG alteration and practical concerns, and close partnership with the neurophysiologist enables meaningful interpretation of the available data.

References

Absalom AR, Mani V, et al. 2005. "'Paedfusor' pharmacokinetic data set." *Br J Anaesth* 95:110.

Bray, R. J. 1998. "Propofol infusion syndrome in children." *Paediatric Anaesthesia* 8 (6):491-9.

Constant, I., and A. Rigouzzo. 2010. "Which model for propofol TCI in children." *Paediatric Anaesthesia* 20 (3):233-9.

Drover, D., and H. R. Ortega. 2006. "Patient state index." *Best Practice & Research. Clinical Anaesthesiology* 20 (1):121-8.

Fulkerson DH., Satyan KB, et al. 2011. "Introperative monitoring of motor evoked potentials in very young children." *J Neurosurg Pediatrics* 7:331-337.

Furay, C., and T. Howell. 2010. "Paediatric neuroanaesthesia." *Continuing Education in Anaesthesia Critical Care & Pain* 10 (6):172-176. doi: https://www.sciencedirect.com/science/article/pii/S1743181617303347?via%3Dihub.

Hermanns H, Lipfert P, et al. 2006. "Propofol infusion syndrome during anaesthesia for scoliosis surgery in an adolescent with neonatal progeroid syndrome." *Acta Anaesthesiol Scand* 50 (3):393-394.

Kandil, A. I., C. S. Pettit, L. N. Berry, V. O. Busso, M. Careskey, E. Chesnut, D. W. Buck, N. D. Leslie, J. Tamai, J. J. McAuliffe, and V. Chidambaran. 2019. "Tertiary Pediatric Academic Institution's Experience With Intraoperative Neuromonitoring for Nonspinal Surgery in Children With Mucopolysaccharidosis, Based on a Novel Evidence-Based Care Algorithm." *Anesthesia & Analgesia* 09:09.

Kataria BK, Ved SA, et al. 1994. "The pharmacokinetics of propofol in children using three different data analysis approaches." *Anesthesiology* 80:104-122.

Lee, K. H., Y. H. Kim, Y. J. Sung, and M. K. Oh. 2015. "The Patient State Index is well balanced for propofol sedation." *Hippokratia* 19 (3):235-8.

Levin, D.N., S. Strantzas, and B.E. Steinberg. 2019. "Intraoperative neuromonitoring in paediatric spinal surgery " *BJA Education* 19 (5):165-171.

Lewis, S. J., I. H. Y. Wong, S. Strantzas, L. M. Holmes, I. Vreugdenhil, H. Bensky, C. J. Nielsen, R. Zeller, D. E. Lebel, M. de Kleuver, N.

Germscheid, A. Alanay, S. Berven, K. M. C. Cheung, M. Ito, D. W. Polly, C. I. Shaffrey, Y. Qiu, and L. G. Lenke. 2019. "Responding to Intraoperative Neuromonitoring Changes During Pediatric Coronal Spinal Deformity Surgery." *Global Spine Journal* 9 (1 Suppl):15S-21S.

Lyon, R., J. Feiner, and J. A. Lieberman. 2005. "Progressive suppression of motor evoked potentials during general anesthesia: the phenomenon of "anesthetic fade"." *Journal of Neurosurgical Anesthesiology* 17 (1):13-9.

N, Constant I and Sabourdin. 2012. "The EEG signal: a window on the cortical brain activity." *Pediatric Anesthesia* 22:539-552.

Nimmo AF, Absalom AR, et al. 2018. "Guidelines for the safe practice of total intravenous anaesthesia (TIVA)." *Anaesthesia*. doi: 10.1111/anae.14428.

Parke TJ, Stevens JE, et al. 1992. "Metabolic acidosis and fatal myocardial failure after propofol infusion in children: five case reports." *British Medical Journal* 305 (6854):613-616.

Rigouzzo, A., F. Servin, and I. Constant. 2010. "Pharmacokinetic-pharmacodynamic modeling of propofol in children." *Anesthesiology* 113 (2):343-52.

Sadhasivam S, Ganesh A, et al. 2006. "Validation of the bispectral index monitor for measuring the depth of sedation in children." *Anesth Analg* 102 (2):383-388.

Sala F, Coppola A, Tramontano V. 2015. "Intraoperative neurophysiology in posterior foss tumor surgery in children." *Child's Nerv Syst* 31:1791-1806.

Sala, F., M. J. Krzan, and V. Deletis. 2002. "Intraoperative neurophysiological monitoring in pediatric neurosurgery: why, when, how?" *Childs Nervous System* 18 (6-7):264-87.

Schneider, G., A. W. Gelb, B. Schmeller, R. Tschakert, and E. Kochs. 2003. "Detection of awareness in surgical patients with EEG-based indices--bispectral index and patient state index." *British Journal of Anaesthesia* 91 (3):329-35.

Vasile B, Rasulo F, et al. 2003. "The pathophysiology of propofol infusion syndrome: a simple name for a complex syndrome." *Intensive Care Medicine* 29:1417-1425.

Wilne SH, Dineen RA et al. 2013. "Identifying brain tumours in children and young adults." *BMJ* 347. doi: 10.1136/bmj.f5844.

Yang Y, Huang Z, et al. 2012. "Improving successful rate of transcranial electrical motor-evoked potentials monitoring during spinal surgery in young children." *Eur Spine J* 21:980-984.

Yu Wing-hay H, Chung Chun-kwong E. 2019. Introduction to Intraoperative Neurophysiological Monitoring for Anaesthetists. *Anaesthesia Tutorial of the Week*.

CHAPTER 11

PRE-OPERATIVE ASSESSMENT

EMMA-JANE SMITH

Introduction

Modern pre-operative assessment comprises both information gathering and dispensing. Most UK hospitals now operate a system of pre-assessment clinics (PACs), by which most patients are systematically reviewed by experienced staff (often of nursing background) according to local protocols and given standardised advice on preparing for surgery. Patients identified as higher risk are referred to anaesthetists for in-depth review, consideration of further investigations, and formal risk stratification. At the time of writing, the coronavirus (COVID-19) pandemic has forced the deferral of many elective procedures, with many pre-operative assessments being via telephone as services gradually resume. As neurological procedures involving intraoperative neuromonitoring (IONM) are generally of at least intermediate risk, neuro-anaesthetists often routinely see elective patients themselves in combined PACs, alongside neurosurgeons, clinical nurse specialists and other members of the multidisciplinary team, as required. As well as opportunity for history-taking and examination, this encounter enables the anaesthetist to establish a rapport with the patient, and to provide them with appropriate reassurance. For patients undergoing urgent surgery, pre-assessment takes place on the inpatient wards, often on the day of surgery. Emergency patients might require assessment in the Emergency Department or even the theatre complex itself, in the case of a time-critical tertiary transfer, although such procedures are less likely to involve the use of IONM. Whatever the mode and tempo of presentation, the anaesthetist must assimilate essential information pertaining to the patient, pathology and procedure in order to optimise where possible, plan the most appropriate anaesthetic technique, and guide peri-operative care effectively.

History-taking

History of presenting complaint

The patient's neurological diagnosis and management thus far must be determined, along with the current neurological deficits (peripheral and/or central), and events leading to the proposed procedure. A history of seizures, or epilepsy, is both common in the neurosurgical population and a relative contra-indication to certain modes of IONM; it also affects the choice of anaesthetic and analgesic drugs. Establish whether the seizures are generalised or focal, their frequency and precipitants, as well as drug therapy and its efficacy. If a patient is presenting with a recurrence or metastasis of malignant disease, note carefully their previous treatment, which may have included chemotherapy or radiotherapy, and therefore have an impact on difficulty of intravenous access or airway management, for example. In the case of spinal lesions, bladder and bowel function may be affected. Elicit any neuropsychiatric concerns related to the primary pathology. Ask about symptoms of raised intracranial pressure (ICP) such as headache (worse in the morning and on coughing), nausea and vomiting. Patients with longstanding hydrocephalus have often undergone repeat cerebrospinal fluid (CSF) diversions and other procedures and are frequently well-versed in anaesthetic techniques; the anaesthetist should take a collaborative approach with the patient in planning their peri-operative care.

Past medical history

The presence of comorbidities—especially cardiorespiratory, conferring higher peri-operative risk—must be documented. Look for reduced respiratory reserve in spinal conditions such as scoliosis and ankylosing spondylitis, which may cause restrictive defects. Assess the patient's risk of obstructive sleep apnoea (OSA) with a tool such as STOP-BANG (Chung, Abdullah, and Liao 2016); hypertension and obesity frequently co-exist with this condition. A myocardial infarction in the preceding six months is often seen as a relative contra-indication to surgery, but as many neurosurgical procedures are not elective, the relative risks need to be balanced. Compromised cardiac function may mean that the patient is less well equipped to tolerate the postural effects of the sitting position for neurosurgery. Diabetes is an important comorbidity: look for evidence of macro- and microvascular complications, and quality of glycaemic control; pre-existing peripheral neuropathy should be documented carefully. Aim to

place patients with diabetes first or early on the operating list where possible. Musculoskeletal problems should be explored as they may impede, or be worsened by, intended intra-operative positioning. Explore the patient's exercise tolerance, and what it is limited by (e.g. shortness of breath, chest pain, or pain elsewhere); attempt to objectively quantify this in terms of Metabolic Equivalents (METs) if possible. Patients with end stage renal failure need particular assessment. Dialysis on the day before surgery is prudent where possible; if performed on the day of surgery, large fluid shifts and haemodynamic instability may be anticipated.

Anaesthetic history

Details of previous anaesthetics, both from the patient and previous anaesthetic charts, are extremely informative. Ask the patient about any known issues with previous anaesthetics, such as with intubation, drug reactions, or severe postoperative nausea and vomiting (PONV). Occasionally a patient may be carrying an "Airway Alert" card (Difficult Airway Society 2018) or have such a warning displayed prominently on their medical record. Ask about dental problems and gastro-intestinal reflux.

Drug history

A complete drug history must be documented, including over-the-counter and complementary/alternative medicines. Particularly problematic drug classes in neurosurgery are the anticoagulants and antiplatelets, which require careful consideration of reversal, mitigation and timing of surgery between the surgeon, anaesthetist and haematologist. The critical-site nature of neurosurgery means that many patients are unsuitable for pharmacological thromboprophylaxis, and so the intra-operative use of thromboembolic deterrent stockings and pneumatic calf compression devices is essential. Conversely, oestrogen-containing medications such as the oral contraceptive pill and hormone replacement therapy should be stopped one month prior to elective surgery, as they carry a high risk of thromboembolism.

Chronic painkillers should be continued, as the patient is dependent upon this background and to remove it will guarantee an analgesic deficit at best and risk withdrawal at worst. Particular attention should be paid to opioid-releasing patches and their schedule of changes. Involve the local pain team service early in the care of such patients.

The peri-operative management of antihypertensive agents needs careful consideration. It is common practice to avoid angiotensin-converting

enzyme inhibitors and angiotensin-II receptor blockers on the morning of surgery as they may be associated with refractory hypotension under general anaesthesia; however, this is controversial. Beta-blockers should be continued (and perhaps even started) in patients at high risk of peri-operative cardiac events.

Neurosurgical patients are often prescribed steroids to reduce inflammation at critical sites, and these should be continued along with gastroprotective agents. Additional intra-operative steroid cover may also be necessary, depending upon dose and duration (Woodcock et al. 2020). Steroids frequently worsen glycaemic control in patients with diabetes and may necessitate a peri-operative variable-rate insulin infusion.

Anticonvulsants are another commonly encountered drug class in these patients, and are associated with narrow therapeutic indices, drug interactions and side effects related to P450 enzyme induction or inhibition. For example, phenytoin and carbamazepine increase metabolism of the aminosteroid neuromuscular blocking drugs such as rocuronium. For acutely prescribed anticonvulsants, take note of the dosage administered as it may have been inadequate in relation to body weight.

With regard to allergies, be aware that patients with chronic conditions and frequent hospital presentations (spina bifida being a good example) have a high prevalence of acquired latex allergy (Alenius et al. 1994). A history of allergy to fruits may also be elicited, suggestive of latex-fruit syndrome (Wagner and Breiteneder 2002). These patients should be operated on first on the list where possible, or after a prolonged “resting” period of the theatre after the removal of natural latex products. Another substance gaining recent attention as an allergen is chlorhexidine, which is present in a large number of products (e.g. surgical preparation solution) and devices (e.g. central venous catheters). Anaphylaxis to chlorhexidine may present insidiously and represent a serious diagnostic challenge under anaesthesia (Rose et al. 2019). Document the nature and severity of all allergies, particularly to penicillin; this may enable the safe use of cephalosporins in patients with mild reactions. Allergy to iodine (or shellfish) is relevant to the use of surgical skin preparation and contrast agents. Reactions to plasters and tape should be noted as this may influence the materials chosen to secure IONM electrodes.

Social history

Social history should include a quantification of alcohol intake and smoking in units and pack-years respectively. Ask about illicit drug use. Most importantly, establish the patient's baseline functional status. Are they working, and in what field? Do they drive (or has this been precluded by their current problems)? If unsafe to drive, check that they have reported this to the DVLA. Where do they live (home, residential care home, nursing home, other) and with whom? Do they have stairs, and are they capable of climbing them? What activities of daily living can they perform by themselves? Do they have a package of care? It is helpful to establish a baseline frailty score (Rockwood et al. 2005) and/or performance status.

Family history

Take note of any neurological conditions that have a hereditary predisposition, such as epilepsy. A family history of anaesthetic problems might rarely suggest a critical anaesthetic condition such as suxamethonium apnoea or malignant hyperthermia.

Collateral history

In the case of emergency or paediatric patients, or in severe cognitive impairment, a history may need to be obtained from collateral sources, such as the patient's relatives, medical records or GP. In trauma patients, the goal is a focused history using the acronym AMPLE (allergies, medications, past medical history, last meal and events leading to presentation) (American College of Surgeons 2018). Previous anaesthetic charts are an invaluable source of information, as are pre-hospital records, which give an indication of the scene from which the patient was retrieved, and likely pattern of associated injuries in trauma cases. It is, however, unusual for IONM to be used in such acute situations.

Examination

Airway

An assessment must be made of the patient's airway, including mouth opening, jaw slide, dentition, neck movement and Mallampati score; this will enable anticipation of difficult face mask ventilation, intubation, or both, in many (but not all) cases. Neck movement is particularly pertinent

in patients with cervical pathology; the neck may be fixed or unstable, and avoidance of excessive movement during airway manipulation may be facilitated by videolaryngoscopy or fibreoptic intubation. Other specific conditions seen in neurosurgical patients, such as acromegaly, carry a higher risk of difficult airway management and patients should be warned accordingly. If a nasal intubation is planned, base of skull fractures and CSF leaks must be excluded (such as in a trauma patient); in the elective setting, assessment of nostril patency can be useful.

Cardiorespiratory

A focused cardiorespiratory examination is indicated, particularly in elderly patients, those with a strong smoking history, known chronic cardiorespiratory disease, or patients with neurosurgical conditions associated with compromise in these systems (e.g. scoliosis). Make particular note of the patient's baseline blood pressure, as this will inform intra-operative blood pressure targets, especially in the face of chronically altered cerebral autoregulation. Certain patients are occasionally deliberately "hypertensed" in the acute scenario, such as in traumatic brain injury prior to the placement of an ICP monitoring device, or in the presence of vasospasm.

Neurological

The anaesthetist should make careful note of pre-existing neurological deficits and may wish to ratify these themselves. This examination may include peripheral motor and sensory function, cranial nerve function, level of consciousness (Glasgow Coma Scale (GCS)), pupil size and reactivity. The GCS, whilst not a perfect tool, is particularly relevant in terms of its motor component, and the trend it follows; it also correlates well with in-hospital mortality in the trauma population (Moore et al. 2006). A precipitous decline may indicate new or worsening pathology and require urgent investigation and intervention. A GCS below 8 is the conventional threshold for intubation and mechanical ventilation, as it frequently coincides with airway compromise; however, the clinical situation is much more important than an isolated number in this regard. Patients with raised ICP may have a readily apparent third or sixth cranial nerve palsy; brainstem lesions are another common cause of cranial nerve deficit, and impaired gag or cough reflexes will place the patient at risk of regurgitation and aspiration of stomach contents. Fluctuating neurological deficits may be caused by pathology of vascular origin, whereby the patient is dependent upon a certain blood pressure; this may especially be seen in vasospasm. High

cervical disease will impede phrenic nerve function (C3, 4 and 5) and cause corresponding loss of the diaphragmatic contribution to respiration.

Patients undergoing major intracranial surgery encroaching on eloquent brain regions are assessed pre-operatively by a neuropsychologist, who may analyse memory function, attention span, spatial perception and higher cognition.

Other

Acute trauma patients require a formal primary and secondary survey (Glen et al. 2016) and the anaesthetist must be cognisant of their findings. The cervical spine may be immobilised, which may necessitate manual in-line stabilisation to minimise movement during airway manipulation.

Finally, ensure that an accurate height and weight are recorded for the patient, as this will be required to accurately set up total intravenous anaesthesia (TIVA). In extremes of BMI it pays to consider the ideal (or adjusted) body weight in advance.

Investigations

The investigations already performed for a patient with a neurosurgical diagnosis typically focus on imaging. The anaesthetist should note these scans but not hesitate to request further tests as required. The National Institute for Health and Care Excellence (NICE) has produced guidance on pre-operative investigations in elective patients (National Institute for Health and Care Excellence 2016); recommendations are broadly based on the patient's premorbid status and level of surgery. Such guidance should be interpreted in light of a patient's individual circumstances.

Blood tests

Neurosurgical operations can be associated with significant blood loss; the anatomical compartments involved are not distensible and so haemorrhage in these areas may result in serious functional deficits. A baseline haemoglobin is essential, and anaemia should be corrected in the elective setting; request haematinics including iron studies, vitamin B12 and red cell folate levels as indicated. Haemoglobinopathies such as sickle cell disease should be screened for in patients with a suggestive family history or compatible ethnicity.

There is an obvious need to exclude or manage any pre-existing bleeding tendency in the neurosurgical population. Standard platelet count and coagulation screening is essential; visco-elastic haemostatic tests such as thrombo-elastography (TEG) and rotational thrombo-elastometry (ROTEM) may be available in certain centres.

The white cell count may indicate infection but is often raised in steroid therapy. C-reactive protein is raised in a variety of infective and inflammatory pathologies, including malignancy. Procalcitonin is a more recently introduced biomarker which is raised in bacterial and fungal infections and has gained popularity in the critical care setting.

Electrolyte disorders are common in the neurosurgical population, particularly disorders of sodium imbalance, which are associated with pronounced changes in brain volume. Paired serum and urinary osmolarities are needed to discriminate between diabetes insipidus, the syndrome of inappropriate anti-diuretic hormone, and cerebral salt wasting. Renal insufficiency is important to detect as it influences drug choice and dosing, both intra- and postoperatively, and the use of contrast in peri-operative imaging; it is also a relative contra-indication to induced hypotension intra-operatively.

Liver function tests are indicated in patients taking anticonvulsants, as they may cause derangement. Albumin gives an indication of the patient's nutritional status but is also a negative acute phase reactant; its level affects the free fraction of protein-bound drugs. Recent anticonvulsant drug levels should be available.

A bone profile is prudent, as hypocalcaemia is a risk factor for seizures and arrhythmias.

Glycated haemoglobin (HbA1c) should be measured in patients with diabetes mellitus, as a marker of longer-term disease control. Point-of-care glucose testing is also indicated.

In patients with pituitary pathology, endocrine investigations such as cortisol, prolactin and thyroid function should be performed; hormone therapy is instituted pre-operatively and may require peri-operative supplementation.

Cardiovascular

A resting 12-lead ECG is a rapid and simple bedside test and should be performed in the majority of patients, certainly with any cardiovascular risk factor, or over the age of 40 (men) or 50 (women). It will detect ischaemia

and arrhythmia and provide a baseline to compare with postoperative recordings. Patients in whom hypotensive anaesthesia may be required (for example, in trans-sphenoidal surgery) should have a baseline ECG recorded regardless of their personal cardiovascular risk. A transthoracic echocardiogram may be required in patients suspected of, or known to have, valvular or ventricular dysfunction. It may also detect a patent foramen ovale or a septal defect, which are absolute contra-indications to the sitting position for surgery due to the risk of fatal paradoxical air embolism. In the case of patients presenting for carotid endarterectomy (where IONM is often employed for the avoidance of peri-operative stroke), carotid ultrasound scanning should be performed to determine the extent of contralateral stenosis, as this predicts a higher risk of ischaemia with carotid cross-clamping.

Ischaemic heart disease may have previously been investigated with exercise or pharmacological stress testing (to determine reversibility, and therefore likelihood of benefit from percutaneous or surgical revascularisation) or coronary angiography (the gold standard investigation, potentially therapeutic as well as diagnostic). Consultation with a cardiologist is advisable for patients with significant cardiovascular disease needing neurosurgery.

Functional capacity can be formally quantified using cardiopulmonary exercise testing (CPET), although this is a resource-intensive investigation and not widely available.

Respiratory

Patients with significant respiratory disease may benefit from spirometry, on a case-by-case basis. This can identify an obstructive (e.g. asthma, COPD) or restrictive (e.g. from spinal dysmorphism) defect, and possibly track the postoperative improvement of the latter, but the overall effect on outcomes is uncertain. A baseline peak expiratory flow rate should be established in patients with asthma. The utility of a baseline chest X-ray is controversial and should be reserved for cases of marked pulmonary or cardiac disease. Pre-operative arterial blood gases are seldom required unless the patient has extensive respiratory disease or is awaiting neurosurgery as a critical care inpatient. Patients with a history suggestive of OSA may benefit from nocturnal oximetry and/or formal sleep studies, if time to surgery allows.

Infection screening

Universal methicillin-resistant Staphylococcus aureus (MRSA) screening has been the standard of care for some time now, and this is crucial as a positive or still pending result will necessitate significant alterations to the patient pathway. These include isolation, different peri-operative prophylactic antibiotics, and deep cleaning of the theatre after the procedure. With many emergency neurosurgical patients being transferred to tertiary centres as inpatients, nosocomial infection is an important concern and therefore screening should be performed promptly on arrival. This may include screening for other resistant organisms, according to local protocols.

COVID-19 screening is now standard for all admissions; many hospitals have developed so-called "green" or "COVID-secure" pathways, by which a patient (and their household, if they do not live alone) self-isolates at home for a number of days prior to admission to hospital. Such patients are cohorted to designated areas within the hospital, in an effort to avoid hospital-acquired coronavirus disease, which carries a high mortality.

Neurological

A plethora of CT and MRI scans may be available, upon which the surgeons will base their approach, often augmented by intra-operative guidance systems. The anaesthetist should pay attention to the type of pathology, its location and the presence of hydrocephalus and mass effect. Pneumocephalus may be seen postoperatively, in the presence of trauma or CSF leaks, and its presence is a contra-indication to the use of nitrous oxide if the patient requires further surgery. If neuro-angiography has been performed pre-operatively, this will be of critical importance to the anaesthetist as it will define the vascularity of a lesion and which vessels are involved; this in turn informs whether evoked potential IONM is indicated, and if so, which modality. The presence or absence of cross-filling predicts the risk of cross-clamp-related cerebral ischaemia in carotid endarterectomies. In arteriovenous malformations, a venogram provides information on the risk of bleeding. Patients with this pathology may undergo pre-operative embolisation in order to reduce the risk of haemorrhage at subsequent open surgery; however, it does itself carry a risk of bleeding, inadvertent occlusion of functional vessels, and cerebral oedema. Temporary balloon occlusion may be performed by an interventional radiologist on an awake patient in order to inform the surgeon whether or not it is safe to occlude a particular vessel. Should an acute neurological deficit occur, the balloon would be immediately deflated and the risk of

haemorrhage at subsequent operation would rely on induced systemic hypotension instead. Coronary and renal disease are relative contra-indications to the latter approach.

If embolisation has been performed pre-operatively, it is important to note the extent to which it has been effective. This also assists with the planning of vascular access and other devices required, such as rapid infusors and cell salvage.

Other tests

A urinary beta human chorionic gonadotrophin (beta hCG) test is mandatory to exclude pregnancy in females of child-bearing age.

Peri-operative planning

Risk assessment

Peri-operative risk may be estimated using a variety of tools. The most frequently referred to is the American Society of Anaesthesiologists' (ASA) Physical Status Classification System, which was originally devised in 1941 (Saklad 1941) and assigns patients to one of six groups according to comorbid status. This categorisation is relatively subjective and not specialty-specific, but nonetheless has become a conventionally recorded metric in operating theatres worldwide as it permits ease of communication between clinicians and broadly correlates with peri-operative morbidity and mortality. A relatively recent systematic review demonstrated a correlation between ASA class and outcome in elective cranial neurosurgery amongst its constituent studies (Reponen, Tuominen, and Korja 2014).

Another scale that has stood the test of time is the Karnofsky Performance Status (KPS) (Karnofsky and Burchenal 1949), which pre-operatively scores patients between 0 (deceased) and 100 (fully functional). This predicts early morbidity in elective craniotomy patients, with scores of 80 and above generally being associated with favourable neurological outcomes, and 70 and below poorer neurological outcomes and non-neurological complications (Reponen, Tuominen, and Korja 2014).

Both ASA and KPS, along with three other variables (patient sex, tumour location and severity of oedema) form the "SKALE" grading system (Sacko et al. 2007), but this was only proposed for use in elderly patients with meningioma, and has not been prospectively validated. A further functional

status-based score is the Modified Rankin Scale (Rankin 1957), which was developed for use in a stroke population but has weak evidence for use in patients undergoing craniotomies (Reponen, Tuominen, and Korja 2014).

Finally, the Charlson comorbidity score, originally developed to predict 10-year survival in a medical population (Charlson et al. 1987), may correlate with neurosurgical outcomes according to retrospective data (Reponen, Tuominen, and Korja 2014) but is more complex.

None of these scoring systems can provide a risk prediction on an individual patient level; tools such as POSSUM (Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity) (Copeland, Jones, and Walters 1991) are designed for this purpose and are in use in other surgical specialties, but require intra-operative data and so cannot be used for truly pre-operative risk estimation. Tools available for specific assessment of peri-operative cardiac risk include the Revised Cardiac Risk Index (RCRI) (Lee et al. 1999) and the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) online surgical risk calculator (American College of Surgeons 2020) (Bilimoria et al. 2013). Cardiovascular risk stratification and mitigation of non-surgical complications in the neurosurgical population has been the topic of a recent review (Algahtani and Merenda 2020). Tomlinson et al proposed a pre-operative frailty score for early postoperative morbidity and mortality in cranial neurosurgery, determining their variables from retrospective interrogation of the NSQIP database (Tomlinson et al. 2017). After multivariate analysis, the most significant factors associated with mortality (and therefore the most heavily weighted in the proposed model) were the presence of ascites (52.4% mortality), pre-operative ventilator dependency (31.5%), and renal failure (38.5%).

Risk prediction tools must be used with caution, as complications and death are binary on the scale of an individual patient: they either occur or they do not. Clinicians should have an honest discussion with the patient and their loved ones about the risks involved.

Consent

Patients will be taken through a written consent process by their neurosurgeon, and this will often include mention of "anaesthetic risk". This is of course no substitute for a thorough verbal consent process as part of the anaesthetic consultation, and although a consent form is not required, the anaesthetist should note the details of the conversation in the anaesthetic

record. General anaesthetic and theatre procedures should be outlined, including the pre-operative safety checks (which may be repetitive and unsettling for patients), the institution of standard monitoring and venous access, and where the patient will go to sleep (anaesthetic room versus theatre) and wake up (theatre versus critical care unit). Gain verbal consent for any additional devices the patient may wake up with in situ, such as further peripheral venous and arterial access, central venous access, surgical drains and urinary catheters.

Standard anaesthetic risks should be mentioned, including sore throat, dental damage, itching and shivering, drug reaction and PONV, the last of which notoriously causes as much or even greater distress than pain. Reassure the patient by discussing standard mitigations for each of these common side effects, such as prophylactic anti-emetics and intravenous fluids. If a rapid sequence induction is indicated, warn the patient of the use of cricoid force if appropriate. Discuss the possibility of blood transfusion; this is particularly pertinent in the case of Jehovah's Witnesses, with whom an exhaustive list of blood products and techniques (such as cell salvage) should be explicitly checked for acceptability, and detailed written confirmation obtained.

The individualised pain management plan should be discussed in detail, including pre-operative analgesic loading, continuation of longstanding analgesics, extra medications given intra-operatively and the postoperative plan, including patient-controlled analgesia strategies where indicated. Regional anaesthesia is infrequently performed for neurosurgical operations, as by its nature it induces a deliberate sensory deficit which can cause clinical obfuscation of the underlying pathology; a notable exception is scalp blocks for craniotomies.

Specific concerns for neuro-anaesthesia with IONM include a higher risk of intra-oral damage and myalgia from induced muscular contractions; the patient should be warned of this. The risk of awareness under general anaesthesia (AAGA) should be discussed, especially as TIVA is commonly used, and carries a higher risk of this complication compared to conventional volatile-based anaesthesia (Cook et al. 2014). Reassure the patient by mentioning the depth of anaesthesia (DOA) that will be used to mitigate this risk. Depending on the nature of IONM to be used, needle electrodes may be placed in various anatomical locations; these can cause pinprick (or more significant) bleeding and the patient should be forewarned of this, as well as the likely electrode sites.

If the patient is to be positioned prone, the unusual but serious risk of visual loss should be discussed, as well as facial and tongue swelling, and damage to skin and peripheral nerves. The sitting position with flexed head can rarely, but devastatingly, be associated with postoperative tetraplegia. These are good examples of material risks to which a reasonable person would attach significance, and which doctors therefore have a duty to disclose to patients regardless of rarity (Chan et al. 2017) (Heywood 2015).

Wake-up testing, or asleep-awake-asleep procedures, require special discussion. The latter is typically indicated when eloquent brain (especially the speech area) is located within the surgical field. This technique requires a well-informed and carefully-selected patient who has been given ample time to ask questions. Psychological and speech and language therapy input is essential, as is briefing the patient on the situation they will find themselves in: immobilised in a Mayfield clamp, needing to remain still and calm, whilst engaging with simple tests of brain function, such as counting or reading cards (or in rarer cases, playing an instrument (King's College Hospital 2020). Wake-up, or Stagnara, testing is less commonly used since the advent of IONM, but still sometimes defaulted to if evoked potential monitoring proves equivocal; scoliosis correction is one such procedure where wake-up testing may be required.

It is also possible that the patient may not be able to provide informed consent due to the nature of their underlying pathology. In this scenario, efforts should be made to contact and involve the patient's next of kin in the decision-making.

Helping patients prepare

When seeing an elective patient in advance, reinforce the advice to bring in all their medications in their original containers, in addition to a copy of their prescription, when they present for admission. Give clear written advice as to which drugs to stop before surgery, and how many days in advance. Equally important to communicate to the patient (and to the ward staff if an inpatient) is which medications should be given on the day of surgery with a sip of water, even whilst fasting. It is an unfortunate reality that the "nil by mouth from midnight" dogma persists, causing unnecessary discomfort and dehydration, as well as omission of critical medications. Explicitly tell the patient and ward staff that clear fluids are encouraged (not just permitted) until two hours pre-operatively.

Patients should be encouraged to prepare for surgery as if training for a race: both events test human physiology in similar ways. Provide guidance on diet, weight loss, exercise and smoking cessation as needed. Signpost the patient to the "Fitter Better Sooner" patient information page on the Royal College of Anaesthetists' (RCoA) website, which provides leaflets and videos on taking an active role in preparing for and recovering from surgery (Royal College of Anaesthetists 2020). The RCoA website also has a wealth of other information, including risk infographics, frequently asked questions and procedure-specific resources.

Finally, all surgery is anxiety-provoking. Often the single best way to alleviate this is to form a rapport with the patient and reassure them that you will be with them during the entire operation and monitoring them extremely closely.

Surgical planning

Unless entirely familiar with the particular practice of a specific neurosurgeon, it is wise to clarify certain aspects of a given procedure ahead of time. The position of the patient is of course paramount, and combined with the theatre orientation, will inform which side of the patient will be optimal to establish vascular access on (patient factors permitting). Discuss ICP, cerebral perfusion pressure (CPP) and BP targets with the surgeon where appropriate. The likelihood of bleeding and availability of crossmatched blood products should be confirmed; the availability of fluid warmers, cell salvage and rapid infuser should be established.

A discussion should take place at the team brief between the surgical, anaesthetic, scrub and neurophysiological staff as to the theatre set-up, equipment required and order of events (e.g. timing of IONM application). The availability of a postoperative critical care bed should be confirmed, if required.

The anaesthetist should check with the neurophysiologist the modalities of IONM that are to be used, and discuss the anaesthetic technique decided upon (usually TIVA). Neuromuscular blocking agents, if used, should be kept to a minimal dose of a short-acting agent so that by the time surgical preparation is complete, this has been metabolised and motor response monitoring is possible.

Summary

Patients requiring neurosurgery may present in an elective, expedited or emergency manner. Specific pre-operative goals include the optimisation of the patient and their underlying pathology; risk stratification and mitigation where possible; and the planning of postoperative care requirements. The anaesthetist is a key source of information for the patient and their loved ones, for both general aspects of the peri-operative pathway and specific aspects such as IONM and wake-up testing. IONM necessitates certain modifications to anaesthetic technique which influence patient workup and management. A multi-disciplinary approach should be taken to secure the best peri-operative outcomes for these patients.

References

American College of Surgeons NSQIP Surgical Risk Calculator. American College of Surgeons, USA. Accessed 17th September 2020. Available at: https://riskcalculator.facs.org/RiskCalculator/

Alenius, H., V. Kurup, K. Kelly, T. Palosuo, K. Turjanmaa, and J. Fink. 1994. "Latex allergy: frequent occurrence of IgE antibodies to a cluster of 11 latex proteins in patients with spina bifida and histories of anaphylaxis." *J Lab Clin Med* 123 (5):712-20.

Algahtani, R., and A. Merenda. 2020. "Multimorbidity and Critical Care Neurosurgery: Minimizing Major Perioperative Cardiopulmonary Complications." *Neurocrit Care*. doi: 10.1007/s12028-020-01072-5.

American College of Surgeons, The Committee on Trauma. *ATLS® Advanced Trauma Life Support*. 10th Edition ed, *Student Course Manual*. Chicago, USA: American College of Surgeons

Bilimoria, K. Y., Y. Liu, J. L. Paruch, L. Zhou, T. E. Kmiecik, C. Y. Ko, and M. E. Cohen. 2013. "Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons." *J Am Coll Surg* 217 (5):833-42 e1-3. doi: 10.1016/j.jamcollsurg.2013.07.385.

Chan, S. W., E. Tulloch, E. S. Cooper, A. Smith, W. Wojcik, and J. E. Norman. 2017. "Montgomery and informed consent: where are we now?" *BMJ* 357:j2224.

Charlson, M. E., P. Pompei, K. L. Ales, and C. R. MacKenzie. 1987. "A new method of classifying prognostic comorbidity in longitudinal studies: development and validation." *J Chronic Dis* 40 (5):373-83. doi: 10.1016/0021-9681(87)90171-8.

Chung, F., H. R. Abdullah, and P. Liao. 2016. "STOP-Bang Questionnaire: A Practical Approach to Screen for Obstructive Sleep Apnea." *Chest* 149 (3):631-8. doi: 10.1378/chest.15-0903.

Cook, T. M., J. Andrade, D. G. Bogod, J. M. Hitchman, W. R. Jonker, N. Lucas, J. H. Mackay, A. F. Nimmo, K. O'Connor, E. P. O'Sullivan, R. G. Paul, J. H. Palmer, F. Plaat, J. J. Radcliffe, M. R. Sury, H. E. Torevell, M. Wang, J. Hainsworth, J. J. Pandit, Anaesthetists Royal College of, Britain Association of Anaesthetists of Great, and Ireland. 2014. "5th National Audit Project (NAP5) on accidental awareness during general anaesthesia: patient experiences, human factors, sedation, consent, and medicolegal issues." *British Journal of Anaesthesia* 113 (4):560-74.

Copeland, G. P., D. Jones, and M. Walters. 1991. "POSSUM: a scoring system for surgical audit." *Br J Surg* 78 (3):355-60. doi: 10.1002/bjs.1800780327.

Difficult Airway Society. 2018. "DAS Airway Alert Card and Difficult Airway Database." Difficult Airway Society, accessed 17th September 2020. https://das.uk.com/dad.

Glen, J., M. Constanti, K. Brohi, and Group Guideline Development. 2016. "Assessment and initial management of major trauma: summary of NICE guidance." *BMJ* 353:i3051.

Heywood, R. 2015. "R.I.P. SIDAWAY: PATIENT-ORIENTED DISCLOSURE-A STANDARD WORTH WAITING FOR? Montgomery v Lanarkshire Health Board[2015] UKSC 11." *Med Law Rev* 23 (3):455-66. doi: 10.1093/medlaw/fwv024.

Karnofsky, D. A., and J. H. Burchenal. 1949. "The clinical evaluation of chemo therapeutic agents in cancer." In *Evaluation of Chemotherapeutic Agents*, edited by C.M. MacLeod, 191–205. New York: Columbia University Press.

King's College Hospital. 2020. "Patient plays violin while surgeons remove brain tumour." King's College Hospital - NHS Foundation Trust, accessed 27th September 2020.

Lee, T. H., E. R. Marcantonio, C. M. Mangione, E. J. Thomas, C. A. Polanczyk, E. F. Cook, D. J. Sugarbaker, M. C. Donaldson, R. Poss, K. K. Ho, L. E. Ludwig, A. Pedan, and L. Goldman. 1999. "Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery." *Circulation* 100 (10):1043-9. doi: 10.1161/01.cir.100.10.1043.

Moore, L., A. Lavoie, S. Camden, N. Le Sage, J. S. Sampalis, E. Bergeron, and B. Abdous. 2006. "Statistical validation of the Glasgow Coma Score." *Journal of Trauma-Injury Infection & Critical Care* 60 (6):1238-43; discussion 1243-4.

National Institute for Health and Care Excellence. 2016. Routine preoperative tests for elective surgery: NICE guideline [NG45]. London: National Institute for Health and Care Excellence.

Rankin, J. 1957. "Cerebral vascular accidents in patients over the age of 60. II. Prognosis." *Scott Med J* 2 (5):200-15. doi: 10.1177/003693305700200504.

Reponen, E., H. Tuominen, and M. Korja. 2014. "Evidence for the use of preoperative risk assessment scores in elective cranial neurosurgery: a systematic review of the literature." *Anesth Analg* 119 (2):420-32. doi: 10.1213/ANE.0000000000000234.

Rockwood, K., X. Song, C. MacKnight, H. Bergman, D. B. Hogan, I. McDowell, and A. Mitnitski. 2005. "A global clinical measure of fitness and frailty in elderly people." *CMAJ* 173 (5):489-95. doi: 10.1503/cmaj.050051.

Rose, M. A., T. Garcez, S. Savic, and L. H. Garvey. 2019. "Chlorhexidine allergy in the perioperative setting: a narrative review." *Br J Anaesth* 123 (1):e95-e103. doi: 10.1016/j.bja.2019.01.033.

Royal College of Anaesthetists. 2020. Preparing for surgery – Fitter Better Sooner. London: Royal College of Anaesthetists. Accessed 17th September 2020. https://rcoa.ac.uk/patient-information/preparing-surgery-fitter-better-sooner

Sacko, O., M. Sesay, F. E. Roux, T. Riem, B. Grenier, D. Liguoro, and H. Loiseau. 2007. "Intracranial meningioma surgery in the ninth decade of life." *Neurosurgery* 61 (5):950-4; discussion 955. doi: 10.1227/01.neu.0000303190.80049.7d.

Saklad, M. 1941. "Grading of patients for surgical procedures." *Anesthesiology* 2 (3):281-284.

Tomlinson, Samuel B., Keaton Piper, Kristopher T. Kimmell, and G. Edward Vates. 2017. "Preoperative Frailty Score for 30-Day Morbidity and Mortality After Cranial Neurosurgery." *World neurosurgery* 107:959-965. doi: https://dx.doi.org/10.1016/j.wneu.2017.07.081.

Wagner, S., and H. Breiteneder. 2002. "The latex-fruit syndrome. *Biochem Soc Trans* 30(Pt 6):935-40.

Woodcock, T., P. Barker, S. Daniel, S. Fletcher, J. A. H. Wass, J. W. Tomlinson, U. Misra, M. Dattani, W. Arlt, and A. Vercueil. 2020. "Guidelines for the management of glucocorticoids during the peri-operative period for patients with adrenal insufficiency: Guidelines from the Association of Anaesthetists, the Royal College of Physicians and the Society for Endocrinology UK. [Review]."

CHAPTER 12

COMPLICATIONS

SACHA SALAMON WHITE
ADITI NIJHAWAN
REBEKAH LAWRENCE
CHULANANDA GOONASEKERA

Introduction

Present-day intra-operative neuromonitoring (IONM) uses several electrophysiological modalities to monitor the function of the nervous system with the intention of detecting and preventing neurological damage during surgery (Tewari et al. 2018). It is divided into two broad terms: mapping and monitoring. The former discerns the functional topography of neural tissue during an operation using microcurrents, whilst the latter monitors the integrity of neural pathways (Novak and Oberndorfer 2012) (Sala et al. 2010). Both use surface and implanted electrodes, the type and location of these being determined by clinicians and neurophysiologists according to the needs of the particular patient and procedure (Matsuyama et al. 2009).

Peri-operative complications are those that arise during and after a procedure and may be either directly or indirectly related to the use of IONM. Surgical complications in general may be classified according to the Clavien-Dindo scale, illustrated in Table 12-1 (Dindo, Demartines, and Clavien 2004). This universal grading system describes the severity of surgical complications according to the corrective actions that subsequently become necessary. Fortunately, most complications related to IONM are mild. The system does not attribute causation to any particular part of the surgical episode and has some important omissions, including impact on psychological wellbeing and quality of life.

Table 12-1. The Clavien-Dindo classification. Adapted with permission from Dindo, Demartines, and Clavien 2004.

Grade	Definition
I	Deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and/or radiological interventions
II	Requiring pharmacological intervention with drugs other than what is permitted for Grade I complications; blood transfusions and total parenteral nutrition are included
III	Requiring surgical, endoscopic or radiological intervention (Grade IIIa – interventions not under general anaesthesia; Grade IIIb – interventions under general anaesthesia)
IV	Life-threatening complication requiring critical care management (Grade IVa – single organ dysfunction; Grade IVb – multi-organ dysfunction)
V	Death of a patient

This chapter summarises what is currently known about the peri-operative complications of IONM from the relatively few studies that have been reported, and explores results from ongoing work, including qualitative data from the perspectives of clinicians involved in facilitating the technique at our own centre.

Direct complications

Seizures

Motor evoked potentials (MEPs) involve direct cortical stimulation and can provoke seizure activity even in patients with no history of seizure disorder (Davis et al. 2013). During open brain surgery, seizures may be terminated by the application of ice-cold saline directly to the brain by the surgeon (Sartorius and Berger 1998). This may avoid the need for systemic anticonvulsant drugs. Such a focal cooling technique has also been noted to terminate spontaneous epileptiform activity arising from space-occupying lesions (Karkar et al. 2002), although the underlying mechanism in both examples remains poorly understood. A King's College Hospital (KCH) neuro-anaesthetist describes the management of intra-operative seizures:

> *"For a seizure it's easy, the surgeon pours cold saline on the brain and the brain goes to sleep. The other thing is to ask the neurophysiologist to stop stimulating, and the surgeon needs to take the instruments out of the brain and stand back. Then, nearly always, the brain just settles on its own."*

A recent retrospective review of fifty patients undergoing resection of tumours close to the motor cortex assisted by IONM revealed a provoked seizure rate requiring pharmacological intervention of 36% (Cordella et al. 2013). Notably, most of the patients in this series who suffered seizures were undergoing sevoflurane anaesthesia rather than propofol total intravenous anaesthesia (TIVA), which not only has epileptogenic properties compared to the anticonvulsant nature of propofol, but also necessitates the use of higher electrical stimulation intensities. As TIVA is now standard practice in many neurosurgical procedures, seizure rates are likely to be lower than this. Chronic use of anticonvulsant therapy (i.e. established seizure disorder) was associated with a higher likelihood of intra-operative seizures.

In a small case series of thalamic astrocytoma resection, none of the five patients studied suffered intra-operative seizures, although one experienced transient status epilepticus postoperatively (Carrabba et al. 2016), although the very small sample size here limits generalisability of these findings.

Seizures are undesirable for many reasons: the associated uncontrolled patient movement can hinder both functional mapping (leaving the patient vulnerable to potentially avoidable neurological damage) and the surgery itself (risking curtailment or abandonment of the procedure, with a potentially worse outcome). There also exists a small risk of significant injury, especially if the patient is immobilised in a Mayfield skull clamp, as described by two neuro-anaesthetists:

> *"If the whole body is seizing, the head is in pins and they're attached to the table, it's a big risk…people can tear the skin…I've seen a case of fracture and an acute extradural haemorrhage."*

> *"I have had seizures on the table in a patient pinned and prone, and this can lead to tearing of the skin and scalp vessels and potentially cervical spine damage."*

Fortunately, this type of occurrence is rare.

Amnesia

There is an interesting potential link between electrical stimulation and interference with memory consolidation. A recent qualitative enquiry (Lawrence, Jones, and Goonasekera 2020) revealed a possible case of this phenomenon, in a middle-aged patient undergoing elective cervical corpectomy. Upon interview three days postoperatively, he was asked how and why he had come into hospital.

> *"A week ago, I'd be able to tell you. I can't remember what came first, the chicken or the egg. There's not anything about the situation I remember."*

He was unable to recall a number of events prior to the procedure, including how he got to hospital and who discussed the surgery with him. When asked about events after the operation, he had only a vague recollection of waking up on the ward, suggesting an additional element of anterograde as well as retrograde amnesia. The neuromonitoring reports in this case indicated no significant signal changes throughout the procedure, and therefore there no postoperative deficits were anticipated; however, it is possible that the patient's background of heavy alcohol intake may have contributed to his memory loss.

Animal studies are suggestive of similar effects: Gold and colleagues demonstrated that electrical stimulation applied to the brains of rats could elicit amnesia as measured with the use of a 24-hour retention test. However, inducement of seizure was necessary for this amnesia to occur (Gold, Macri, and McGaugh 1973).

Overall, there is very limited literature assessing the independent impact of IONM on amnesia, and more investigation needs to be performed to suggest any causal link between the two.

Visual and motor effects

It is plausible that visual and/or motor side effects may be precipitated by certain forms of IONM due to direct cortical stimulation. Electrical stimulation of the posteromedial cortex and areas directly ventral or dorsal to this can elicit both motor and visual responses, along with somatosensory and cognitive responses (Foster and Parvizi 2017). As such, vigilance should be maintained for such effects when direct cortical stimulation is used as part of IONM.

Cardiac events

Qualitative investigation at our centre has recently revealed a variety of cardiac events in patients undergoing IONM; these underline the importance of withdrawal of the precipitating stimulus. The decision of whether to proceed or abandon following such an event is a multidisciplinary one.

> *"I've never had an asystole or severe bradycardia that hasn't resolved with just removal of all the stimulants."*

> *"I have abandoned when we had asystole. Most of these problems will happen when they're just trying to get the last bit of the tumour out. It will always be a team decision."*

> *"I had a patient go into asystole and [ventricular fibrillation] after stimulation. Luckily both resolved spontaneously, but the risk here is overtreatment and delivery of adrenaline in an open brain situation – on return of spontaneous output the [blood pressure] is raised, and bleeding occurs that may be catastrophic."*

Most of the evidence for cardiac complications in IONM is anecdotal, perhaps reflecting the ethical and systematic difficulties in independently investigating this.

Dental and oral damage

Jaw clenching associated with MEP recording can produce damage to the teeth and oral mucosa (Macdonald 2006); a recent review indicated that oral trauma is in fact the most common complication of MEP IONM (Singh et al. 2016). Case reports exist of serious tongue laceration (Hao, Liu, and Ang 2014); avulsion of teeth is also possible. This risk is mitigated by the routine use of a soft bite block – often a simple roll of gauze. This intervention can also prevent bite-induced deformation and subsequent obstruction of the reinforced (armoured) tracheal tubes which are considered standard in neuro-anaesthesia.

Muscle necrosis

Repeated muscular contractions can lead to breakdown of muscle architecture, with associated systemic hyperkalaemia and lactic acidaemia in severe cases, resembling rhabdomyolysis.

Needle electrodes themselves have also been implicated in a case of compartment syndrome of the upper limb in a patient receiving IONM for vascular surgery (Eli et al. 2018). The patient ultimately required fasciotomies to treat this (a Grade IIIb complication in the Clavien-Dindo classification). Necrosis of the tongue has been described (Singh et al. 2016).

A local anaesthetist highlights the relevance of the patient's muscle mass:

> *"If they're stimulating at a high voltage a lot in a patient who is particularly muscular, complications are more likely compared with patients with no muscle mass."*

Skin marks

As IONM requires surface and implanted electrodes in various anatomical locations, there is potential to leave temporary but noticeable marks on the skin that may cause concern. In a local recent qualitative investigation, one patient commented that she thought the marks left on her skin may have been the result of an accident during the surgical procedure, and so forewarning patients of these marks may help to alleviate postoperative anxiety. This is of particular importance when less common electrode sites are used, such as the anal sphincter, genitals, eye or soft palate.

Skin burns are theoretically possible at electrode sites if electrocautery equipment is faulty (Moller 1992).

Retained electrodes

Sharp corkscrew electrodes placed and removed by the neurophysiologist are often not subject to a strict counting procedure as with other surgical instruments, conferring the risk of retained items, as one anaesthetist describes.

> *"There's the risk of all the electrodes not being taken out at the end of the operation, as these are placed and removed by a single operator without a formal counting process."*

Consideration should be given to incorporating such a count in local surgical sign-out procedures for this reason.

Loss of IONM signals

The intra-operative loss of IONM signals may represent an equipment, anaesthetic or surgical problem; systematic approaches to such a scenario are more fully discussed in other chapters. After an initial assessment and troubleshooting, a decision must be made as to whether to proceed or abandon the procedure, as clinicians at KCH describe.

> *"If something's not working it's probably my fault. Are all my wires connected, is the system working? If all of that is working…I'll check with the anaesthetist: did you change anything? If not, then it's probably the surgeon."* – Neurophysiologist

> *"If signal is lost for some other reason, especially with complications, it is perhaps a good reason to stop further surgery, wake the patient up and come back on another day once a full assessment has been made."* – Neuro-anaesthetist

> *"Occasionally you do have situations where [IONM] is not working very well. And occasionally from the beginning you don't have very good monitoring, but then as soon as you open and do a debulking of the tumour it improves, and that's very reassuring"* – Neurosurgeon

Jain et al (Jain, Khanna, and Hassanzadeh 2015) categorise signal loss into those associated with medical/physical consequences, and those arising due to technical issues. They suggest a stepwise algorithm to manage signal change in spinal surgery. The algorithm (Figure 12-1) covers pertinent factors with a potential to alter IONM signals.

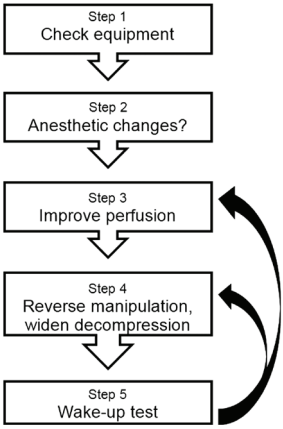

Fig. 12-1. Stepwise algorithm for a change in signal. Reproduced with permission (Jain, Khanna, and Hassanzadeh 2015)

Indirect complications

Awareness

Accidental awareness under general anaesthesia (AAGA) is the later recall by patients of time spent under general anaesthesia. It is detected postoperatively when a patient raises concerns or otherwise undergoes a structured interview, commonly the Brice questionnaire (Brice, Hetherington, and Utting 1970). The 5th National Audit Project (NAP5) studied this phenomenon and reported an overall incidence of approximately 1 in 19,000 anaesthetics; this was subdivided into a 1 in 8,000 risk where neuromuscular blockade was used, and 1 in 136,000 where it was not (Pandit et al. 2014). The need for TIVA in IONM does confer greater risk of AAGA; however, NAP5 found that many incidences of awareness during TIVA were related to under-dosing, contributed to by failing to use a target-controlled infusion (TCI) technique; TCI is, however, standard in neuro-anaesthesia.

Depth of anaesthesia (DOA) monitors employing processed EEG signals are recommended during TIVA, and NAP5 was strongly supportive of the use of such monitoring in this setting. Many neurosurgical centres now use this technology in everyday practice; the various techniques available are discussed elsewhere in this book.

Despite the rarity of AAGA, clinicians must strive to avoid it as it carries significant psychological morbidity. NAP5 found that 51% of patients with AAGA experienced distress and 41% suffered long term adverse effects, including depression, anxiety, post-traumatic stress disorder, complex phobias and flashbacks (Pandit et al. 2014). It is also apparent that the timing of questioning and fear of judgement may contribute to under-reporting of AAGA (Ghoneim 2007). Recall may not occur immediately postoperatively, instead manifesting days or weeks later, when the patient may have been discharged home. It is vital that AAGA be identified so that it may be reported back to the anaesthetist concerned and the patient provided with appropriate psychological support.

Drug extravasation

Extravasation of intravenous fluids or drugs is a risk in any anaesthetic, but is particularly relevant in TIVA, as it risks both tissue necrosis and AAGA. Drug extravasation injuries should be assessed by a plastic surgeon. Serious sequalae of drug extravasation described in the literature include compartment syndrome requiring fasciotomy (Kalraiya et al. 2015) and soft

tissue necrosis requiring debridement (LeBlanc et al. 2014). In both of these cases, propofol was the culprit. Vascular access site vigilance and appropriate setting of infusion device pressure alarms are essential in preventing these complications.

Propofol infusion syndrome

Propofol infusion syndrome (PrIS) was described just before the turn of the millennium in a retrospective review of children receiving propofol (Bray 1998). Severe bradycardia progressing to asystole was seen with infusions over 4 mg/kg/h for a duration of 48 hours or longer. For this reason, PrIS is more likely to be diagnosed postoperatively, for example on the critical care unit, but anaesthetists should carefully calculate intra-operative dosages, nonetheless. Risk factors for PrIS include severe head injury, sepsis, high exogenous or endogenous catecholamine and glucocorticoid levels, low carbohydrate or high lipid intake, and inborn errors of fatty acid oxidation (Loh and Nair 2013). It is common practice to use a volatile agent for propofol sparing purposes in paediatric neurosurgery in order to mitigate the risk of PrIS.

Equipment artefact

IONM modalities involving muscle stimulation can artificially alter DOA monitor outputs, typically increasing the values, with the attendant risk of unnecessarily increased anaesthetic depth. Artefact can also be produced in the ECG, arterial pressure or pulse oximetry traces, mimicking arrhythmia or compromised oxygenation, respectively (Figure 12-2). Artefacts affecting the ECG have also been documented following the use of somatosensory evoked potentials (SSEPs) (Choudhry et al. 1998). One method of preventing this interference is to ensure that the ECG electrodes are positioned away from the stimulating IONM electrodes (Choudhry et al. 1998). Temporarily halting electrical stimulation will permit discrimination between artefact and actual physiological deterioration (Rudigwa et al. 2015).

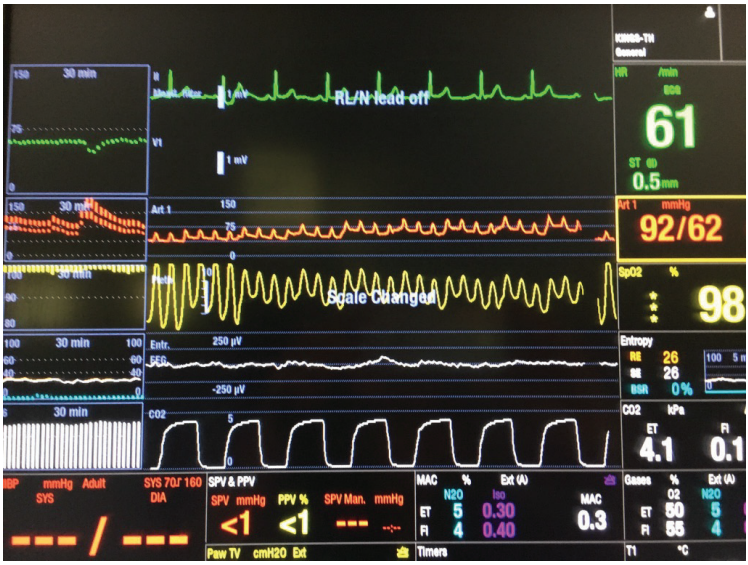

Fig. 12-2. Artefact observed in the arterial pressure and pulse oximetry waveforms during MEP stimulation.

Summary

The peri-operative complications of IONM may be divided into direct and indirect, with the latter mainly concerned with the particular risks associated with TIVA. Most direct complications are caused by muscular contraction associated with the MEP modality. There are few publications on the complications of IONM, with most being case reports or case series. As the technique becomes more widely used, further data are expected to emerge.

References

Bray, R. J. 1998. "Propofol infusion syndrome in children." *Paediatric Anaesthesia* 8 (6):491-9.

Brice, D. D., R. R. Hetherington, and J. E. Utting. 1970. "A simple study of awareness and dreaming during anaesthesia." *British Journal of Anaesthesia* 42 (6):535-42.

Carrabba, G., G. Bertani, F. Cogiamanian, G. Ardolino, B. Zarino, A. Di Cristofori, M. Locatelli, M. Caroli, and P. Rampini. 2016. "Role of

Intraoperative Neurophysiologic Monitoring in the Resection of Thalamic Astrocytomas." *World Neurosurgery* 94:50-56.

Choudhry, D. K., S. A. Stayer, M. A. Rehman, and R. E. Schwartz. 1998. "Electrocardiographic artefact with SSEP monitoring unit during scoliosis surgery." *Paediatric Anaesthesia* 8 (4):341-3.

Cordella, R., F. Acerbi, C. E. Marras, C. Carozzi, D. Vailati, M. Saini, G. Tringali, P. Ferroli, F. Dimeco, A. Franzini, and G. Broggi. 2013. "Risk of seizures during intraoperative electrocortical stimulation of brain motor areas: a retrospective study on 50 patients." *Neurological Sciences* 34 (1):63-70.

Davis, S. F., T. Altstadt, R. Flores, A. Kaye, and G. Oremus. 2013. "Report of seizure following intraoperative monitoring of transcranial motor evoked potentials." *Ochsner Journal* 13 (4):558-60.

Dindo, D., N. Demartines, and P. A. Clavien. 2004. "Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey." *Annals of Surgery* 240 (2):205-13.

Eli, I. M., N. T. Gamboa, J. Guan, and P. Taussky. 2018. "Acute Compartment Syndrome as a Complication of the Use of Intraoperative Neuromonitoring Needle Electrodes." *World Neurosurgery* 112:247-249.

Foster, B. L., and J. Parvizi. 2017. "Direct cortical stimulation of human posteromedial cortex." *Neurology* 88 (7):685-691.

Ghoneim, M. M. 2007. "Incidence of and risk factors for awareness during anaesthesia." *Best Practice & Research. Clinical Anaesthesiology* 21 (3):327-43.

Gold, P. E., J. Macri, and J. L. McGaugh. 1973. "Retrograde amnesia gradients: effects of direct cortical stimulation." *Science* 179 (4080):1343-5.

Hao, T. J., G. Liu, and P. Ang. 2014. "A rare complication of tongue laceration following posterior spinal surgery using spinal cord monitoring: A case report." *Indian Journal of Anaesthesia* 58 (6):773-5.

Jain, A, A.J. Khanna, and H. Hassanzadeh. 2015. "Management of intraoperative neuromonitoring signal loss." *Seminars in Spine Surgery* 27 (4):229-232.

Kalraiya, A. J., S. Madanipour, H. Colaco, and C. Cobiella. 2015. "Propofol extravasation: a rare cause of compartment syndrome." *BMJ Case Reports* 07:07.

Karkar, K. M., P. A. Garcia, L. M. Bateman, M. D. Smyth, N. M. Barbaro, and M. Berger. 2002. "Focal cooling suppresses spontaneous epileptiform

activity without changing the cortical motor threshold." *Epilepsia* 43 (8):932-5.
Lawrence, R., H. Jones, and C. Goonasekera. 2020. "Retrograde Amnesia Associated With Intraoperative Neuromonitoring." *Journal of Neurosurgical Anesthesiology* 05:05.
LeBlanc, J. M., D. Lalonde, K. Cameron, and J. A. Mowatt. 2014. "Tissue necrosis after propofol extravasation." *Intensive Care Medicine* 40 (1):129-30.
Loh, N, W., and P Nair. 2013. "Propofol infusion syndrome." *Continuing Education in Anaesthesia Critical Care & Pain* 13 (6):200-202.
Macdonald, D. B. 2006. "Intraoperative motor evoked potential monitoring: overview and update." *Journal of Clinical Monitoring & Computing* 20 (5):347-77.
Matsuyama, Y., Y. Sakai, Y. Katayama, S. Imagama, Z. Ito, N. Wakao, K. Sato, M. Kamiya, Y. Yukawa, T. Kanemura, M. Yanase, and N. Ishiguro. 2009. "Surgical results of intramedullary spinal cord tumor with spinal cord monitoring to guide extent of resection." *Journal of Neurosurgery Spine* 10 (5):404-13.
Moller, A. R. 1992. "Intraoperative neurophysiological monitoring." *Neurological Research* 14 (3):216-8.
Novak, K., and S. Oberndorfer. 2012. "Electrophysiology and intraoperative neurophysiological monitoring." *Handbook of Clinical Neurology* 104:149-61.
Pandit, J. J., J. Andrade, D. G. Bogod, J. M. Hitchman, W. R. Jonker, N. Lucas, J. H. Mackay, A. F. Nimmo, K. O'Connor, E. P. O'Sullivan, R. G. Paul, J. H. Palmer, F. Plaat, J. J. Radcliffe, M. R. Sury, H. E. Torevell, M. Wang, J. Hainsworth, T. M. Cook, Anaesthetists Royal College of, Britain Association of Anaesthetists of Great, and Ireland. 2014. "5th National Audit Project (NAP5) on accidental awareness during general anaesthesia: summary of main findings and risk factors." *British Journal of Anaesthesia* 113 (4):549-59.
Rudigwa, P., L. B. Elakkumanan, S. Rajan, and M. V. Prakash. 2015. "ECG artefacts mimicking atrial flutter in posterior fossa surgery." *BMJ Case Reports* 28:28.
Sala, F., P. Manganotti, S. Grossauer, V. Tramontanto, C. Mazza, and M. Gerosa. 2010. "Intraoperative neurophysiology of the motor system in children: a tailored approach." *Childs Nervous System* 26 (4):473-90.
Sartorius, C. J., and M. S. Berger. 1998. "Rapid termination of intraoperative stimulation-evoked seizures with application of cold Ringer's lactate to the cortex. Technical note." *Journal of Neurosurgery* 88 (2):349-51.

Singh, H., R. W. Vogel, R. M. Lober, A. T. Doan, C. I. Matsumoto, T. J. Kenning, and J. J. Evans. 2016. "Intraoperative Neurophysiological Monitoring for Endoscopic Endonasal Approaches to the Skull Base: A Technical Guide." *Scientifica* 2016:1751245.

Tewari, A., L. Francis, R. N. Samy, D. C. Kurth, J. Castle, T. Frye, and M. Mahmoud. 2018. "Intraoperative neurophysiological monitoring team's communique with anesthesia professionals." *Journal of Anaesthesiology Clinical Pharmacology* 34 (1):84-93.

CHAPTER 13

THE PATIENT EXPERIENCE

REBEKAH LAWRENCE
ALINA AMIR

Introduction

Modern clinical practice is patient-centred. The paternalistic doctor-patient relationship has long since been superseded by a partnership in which the knowledge and expertise of the clinician, and the ideas, concerns and expectations of the patient, are blended to permit shared decision-making (Figure 13-1). This improves patient understanding, adherence to proposed management plans, and ultimately, outcomes (Stewart et al. 2000).

This chapter reviews the existing literature and recent qualitative enquiry at our own centre around patients' experience of intra-operative neuromonitoring (IONM), placing emphasis upon areas in need of quality improvement.

Information provision

Consent

The signing of a written consent form prior to surgery is conventional practice, yet neither necessary nor sufficient by itself for valid consent. Anaesthetic consent is typically given verbally, and in neuro-anaesthesia will include provision of details of IONM where used; however, formal consent for the use of IONM rests within the written surgical consent process. Valid consent is dependent upon a person's competence to provide the same – that is, that they are able to understand, retain and weigh up information relating to the risks, benefits and alternatives of a proposed intervention, and that they are able to communicate their decision (Moreschi, Leone, and Sabot 2010).

The risks necessary to disclose to a patient were by convention those considered serious or frequently occurring, and in cases of dispute, the information provided was judged on whether the doctor in question had acted in accordance with a responsible body of medial opinion (the Bolam test). However, a landmark case in 2015 set a new precedent for the standard of consent. Nadine Montgomery suffered a complication of vaginal delivery (shoulder dystocia), which ultimately led to her baby receiving insufficient oxygen during birth and subsequently developing cerebral palsy. On review of the facts, this complication, whilst still rare, was more likely in this case for a number of reasons, and a Caesarean birth would have avoided this risk. Neither emphasis of increased risk nor offer of a Caesarean section were made to Mrs Montgomery, who won her case at the Supreme Court of England on the basis that had she been made aware of the "material" risks pertinent to her case, she would have opted for a Caesarean section and therefore avoided the complications she and her baby suffered. Therefore, clinicians are now expected to provide information to patients on any particular risks to which the individual patient may reasonably attach significance (Chan et al. 2017).

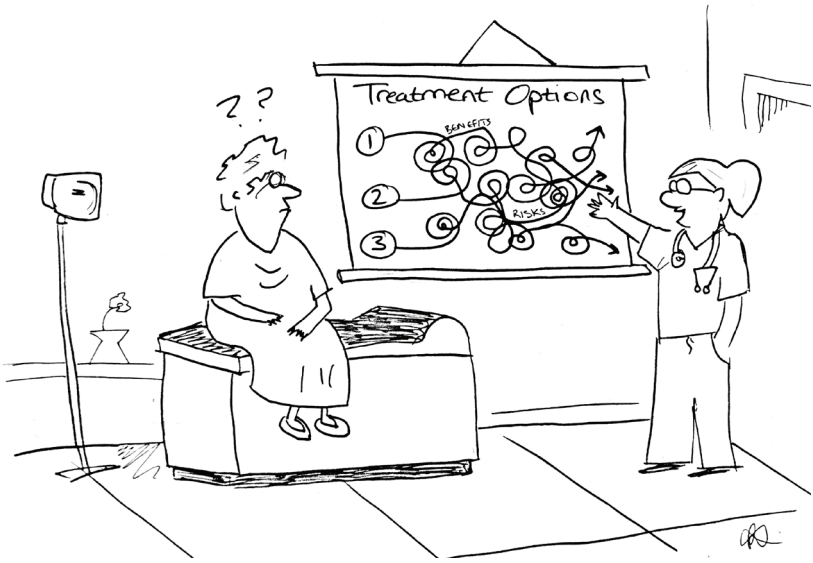

Fig. 13-1. Guiding the patient through ever-increasing medical complexity.

Some patients sign their medical consent form without a full understanding of its contents. This may be the product of one or more reasons: feeling that they have no choice; placing full trust in their medical team to make the right decisions for them; or anxiety around asking questions. It is not uncommon for patients to progress through a treatment plan without a clear understanding of the various advantages and disadvantages, especially those of an ancillary intervention such as IONM.

Understanding and recall

On direct enquiry in the postoperative period, patients who underwent IONM often have very little or no understanding of the technique. These individuals fall into two categories: those who were not provided with adequate information, and those who were, but have subsequently forgotten. The latter is unsurprising; it has been reported that 40-80% of medical information provided by healthcare practitioners in consultations is forgotten immediately (Kessels 2003). This is linked to several factors, including high levels of anxiety, the perceived importance (or not) of the information, and the use of medical jargon. The quantity of information provided to patients, especially around the time of a neurosurgical diagnosis, is also likely to be a contributing factor.

Those patients who do recall some details about IONM tend to have very limited knowledge on the subject. They may vaguely remember parts of the neuromonitoring process and its benefits, but few of the possible risks. One such patient commented,

> *"…they'd got a special probe or something, so when they did the operation, they could check the impulses without waking me up. I thought, 'oh good, I'm so glad!' [laughs]"*

Another patient recalled a little more:

> *"Not the surgeon, but someone else came around and explained there would be four things connected to whatever…is it one on each arm and one on each leg or something? Connecting up to make sure everything's going alright when they're doing the surgery?"*

While these quotes highlight the limited understanding that patients typically retain regarding IONM, the fact that it was seen as a positive intervention used to improve the safety of the surgical procedure resulted in patients being satisfied with this level of knowledge.

Risks

Research shows that IONM has the potential to minimise risk of injury and improve neurosurgical outcomes. However, major modifications to anaesthesia – which carry their own risks, such as awareness under anaesthesia – are required for accurate interpretation. IONM also invites direct complications, including seizures and cardiac events; these are discussed further elsewhere in this book. Crucially, the limitations of IONM mean that its use is not a guarantee of avoidance of intra-operative injury. Patients seldom exhibit understanding of these concepts, yet they would frequently come under the definition of "material" risks as described earlier. Whilst over-emphasising the risks of a procedure can cause concern and increase the potential for refusal of interventions, appropriate amounts of pre-operative information are known to mitigate anxiety and even improve postoperative outcomes (Hathaway 1986). It is therefore essential to strike the correct balance of information provision for the individual person and to allow them to raise any concerns they may have so that these may be addressed.

Information sources

The issue of poor patient understanding of IONM generally stems from inadequacies in the information provided. It is vital to examine these to understand how improvements may be made.

Healthcare professionals

The most common source of information on IONM is the healthcare team involved in a patient's care. This may be one or more of the operating neurosurgeon, neuroanaesthetist, or other professionals such as neurosurgical nurse specialists. Information on IONM, and the associated seeking of consent for its use, may be given during pre-operative assessment in clinic, or less desirably, the night before or morning of surgery. There is little evidence on the best timing, content and team member responsible for such information provision, leading to wide inconsistencies in approach between and within institutions. The neurophysiologist is usually the most knowledgeable team member on the subject but often only comes into contact with the patient in the operating theatre after induction of anaesthesia. The knowledge of the rest of the team must therefore be maintained in order to correctly counsel patients on IONM and its risks.

Patients who undergo IONM are frequently content with the level of information they receive, but this may be confounded by the belief that they have received all the necessary information. A parallel may be drawn with the analytical science concept of 'unknown unknowns', first described by Luft and Ingham in their construction of the Johari window (Luft and Ingham 1955) and later popularised by Donald Rumsfeld in a 2002 US Department of Defense briefing (Rumsfeld 2002). Without the benefit of specialised medical knowledge, patients cannot be expected to be aware of what information they are lacking, or that they lack it at all.

Perhaps understandably, many patients are more concerned with the operation itself rather than additional interventions such as IONM. However, a duty lies with the healthcare team to provide basic information (transforming IONM into at least a 'known unknown') and then tailor further discussion around the patient's desire for more details. This can vary widely between patients, as the individuals below indicate:

> *"I had as much information as I wanted. I'm one of those people who'd rather not know."*

> *"I would have liked to have known a bit more."*

Self-sourced information

Many patients enter the healthcare setting with preconceived ideas and expectations about their treatment. This commonly originates from internet sources and the experiences of friends and family. Internet research unfortunately risks influence by inaccurate or incomplete information, or perhaps even harmful anecdotes that may colour their perception of the technique.

Some patients undergo multiple procedures using IONM during the course of their treatment. Such individuals rely on their past experience as their main source of knowledge for the technique, which naturally shapes their expectations for their upcoming procedure. It is important to inform patients of any alterations in IONM approach that may be necessary for their next procedure.

Guidelines

The British Society for Clinical Neurophysiology (BSCN) produced guidance on IONM in 2013, but this is limited to details of technical

approach and does not mention the topic of information provision to patients (Grover et al. 2019). The American Society of Neurophysiological Monitoring (ASNM) adopted a practice guideline originally published by Skinner (Skinner et al. 2014), which gives recommendations for providing patients with pre-operative information on IONM. It recommends that patients be introduced to their neuromonitoring provider in person or through alternative means of communication, and that information is provided relating to the relevant techniques as well as their risks and benefits. Whilst the UK would do well to introduce similar guidelines, the ever-present strain on the NHS (particularly in the wake of the coronavirus pandemic) may make striving for the same standards challenging. In the meantime, clinicians must use their own judgement to provide the right amount of information to individual patients.

Summary

Patients report a wide range of knowledge and experiences of IONM, both in terms of information provision and recall regarding it, and adverse events resulting from it. Adequate information is a cornerstone of valid consent for any healthcare intervention, and attention must be paid to the material risks for each individual patient.

Very little published guidance exists on the topic of IONM in general, particularly on information provision to patients requiring this technique. As verbal information during consultations is so often forgotten, written patient information to reinforce this discussion would be well-received, and could take the form of a standardised leaflet or web resource.

In certain other surgical specialties, patient cohorting and group provision of standardised pre-operative information is a successful model. Such an approach may be suitable for the dissemination of IONM information to elective patients in the future. The added benefits to this would include being able to ask questions, learning from the answers to others' enquiries, and making contact with a group of people with similar health concerns who may become a significant source of support.

References

Chan, S. W., E. Tulloch, E. S. Cooper, A. Smith, W. Wojcik, and J. E. Norman. 2017. "Montgomery and informed consent: where are we now?" *BMJ* 357:j2224.

Grover, H., P. Walsh, B. Sanders, and C. Shirley. 2019. "Guidelines for Intraoperative monitoring." [English]. British Society for Clinical Neurophysiology, Last Modified 2019, accessed 21st March. http://www.bscn.org.uk/content.aspx?Group=guidelines&Page=guidelines_IOM.

Hathaway, D. 1986. "Effect of preoperative instruction on postoperative outcomes: a meta-analysis." *Nursing Research* 35 (5):269-75.

Kessels, R. P. 2003. "Patients' memory for medical information." *Journal of the Royal Society of Medicine* 96 (5):219-22.

Luft, J. , and H. Ingham. 1955. The Johari window, a graphic model of interpersonal awareness. In *Proceedings of the Western Training Laboratory in Group Development*. Los Angeles: University of California.

Moreschi, C., E. Leone, and A. Sabot. 2010. "[Informed consent and risk management: medico-legal aspects]." *Urologia (Treviso)* 77 Suppl 16:5-10.

Rumsfeld, Donald H. 2002. DoD News Briefing - Secretary Rumsfeld and Gen. Myers. Washington: U.S. Department of Defense.

Skinner, S. A., B. A. Cohen, D. E. Morledge, J. J. McAuliffe, J. D. Hastings, C. D. Yingling, and M. McCaffrey. 2014. "Practice guidelines for the supervising professional: intraoperative neurophysiological monitoring." *Journal of Clinical Monitoring & Computing* 28 (2):103-11.

Stewart, M., J. B. Brown, A. Donner, I. R. McWhinney, J. Oates, W. W. Weston, and J. Jordan. 2000. "The impact of patient-centered care on outcomes." *Journal of Family Practice* 49 (9):796-804.

CHAPTER 14

WHAT WE KNOW AND WHERE TO NEXT

CHULANANDA GOONASEKERA
PEDRO COELHO
HOLLY JONES
CHRISTOPHER CHANDLER

Introduction

This book has presented a multidisciplinary critique on the current status of neurophysiological monitoring and its role in testing the functional integrity of neural structures.

Intra-operative neuromonitoring (IONM) enables a variety of neuronal structures to be monitored, including the cortex, brainstem, spinal tracts, peripheral nerves and neuromuscular junctions (Stecker 2012), but not yet highly sophisticated structures such as the speech area. The overarching goal of IONM is to prevent unexpected neurological deficits following surgery (Sala et al. 2015). It is presumed to reduce the risk of iatrogenic damage to the nervous system, and therefore enable surgeons to achieve the best tumour resection possible with the fewest complications. Signal interpretation requires an excellent working knowledge of neurophysiology, the specific surgical procedure, and the effects of anaesthesia and physiological changes.

There are numerous modalities of IONM. Several are often used together in a single procedure, as each modality provides unique information (Kim et al. 2013) and has different sensitivities and specificities (Rattenni et al. 2015). An inter-professional discussion should take place pre-operatively as to the goals of IONM and the structures at risk, and which modalities are therefore best suited to the individual procedure and patient.

The benefits of IONM are dependent upon its reliability. This requires fulfilment of multiple preconditions, including the provision of a compatible mode of anaesthesia (Cabraja et al. 2009).

The accurate interpretation of IONM requires a cohesive team approach, calling upon the combined experience of neurosurgeons, neuro-anaesthetists and neurophysiologists (Kim et al. 2013). Communication between these professionals is imperative for the successful application of IONM (Stecker 2012).

Some critics argue that IONM lacks a strong evidence base (Sala 2010), and it is true that high-quality studies on the effects of this monitoring on patient outcome are scarce. The literature is conflicting: some investigators find IONM to be an effective means of predicting increased risk of adverse outcomes in spinal surgery (Nuwer et al. 2012), whilst others report its ability to prevent injury to be less than convincing (Sala and Di Rocco 2015). Perhaps the strongest argument against the use of IONM, but also the hardest to prove, is that deficits elicited by the technique may lead to the over-estimation of irreversibly non-functional neural tissue and subsequent resection thereof, when in fact such tissue may have been potentially salvageable.

Signal confounders

Continuous signal integrity is the foundation of sound IONM. The placement and reliable attachment of electrodes is paramount to minimise false positive readings resulting from dislodged monitoring during surgery (Legatt et al. 2016). Keeping all connections tidy to minimise entanglement with equipment or staff is essential.

Gradual attenuation of the electrophysiological signals during lengthy neurosurgical procedures may occur. This phenomenon, “fade”, is more often seen in younger patients and those with spinal cord pathology. The exact mechanisms are not yet understood.

Certain patient factors can make evoked potential recording challenging. These include hypertension, extremes of age, and pre-operative motor or sensory deficits, including the common phenomenon of diabetic neuropathy. In children, immature myelination of nerve tracts may hinder adequate signal transmission for neuromonitoring.

Physiologic factors

A reduction in blood pressure, tissue perfusion, or cerebral blood flow may affect certain modalities of IONM. Even in the presence of normotension, factors such as local pressure from surgical instrumentation or vascular compromise secondary to patient position may precipitate signal change. In such circumstances, a supra-normal blood pressure may be desirable. Particular attention should be paid to the patient's baseline blood pressure, as altered cerebral or spinal perfusion at baseline confers a higher risk of intra-operative ischaemia.

It is important to minimise variations in the partial pressure of oxygen and carbon dioxide, as these can affect signal quality, especially in the presence of altered vascular anatomy.

Core body temperature must be maintained within 2 to 2.5°C of baseline to avoid interference with evoked potentials and EEG. Anaesthetists should exercise caution with infusion of cold intravenous fluids or blood products and be mindful that surgical irrigation can also lead to significant local heat loss and subsequent signal change.

Finally, anaemia must be avoided, and this is simple to monitor with the aid of serial arterial blood gases. Somatosensory evoked potentials (SSEPs) and visual evoked potentials (VEPs) demonstrate increased latency with haematocrits beneath 15%; below 10%, amplitudes also fall.

Patient positioning

Patient positioning for surgery can cause neurologic and/or vascular compromise, but continuous monitoring may be challenging in certain patients. This is especially so when extreme neck flexion is required to enable surgical access. In this scenario, baseline IONM should be performed immediately after induction of general anaesthesia with the patient supine, and once more after positioning for surgery is complete. This enables position to be altered, should signals have deteriorated between baseline and positioning. The team should be aware that position-related signal change may still occur intra-operatively, for example if the patient moves after MEP monitoring.

Anaesthetic effects

In general, the greater the number of synapses through which signals must pass, the more susceptible the modality to signal interference. The most sensitive type of IONM is VEPs (Soghomonyan et al. 2014), and the most resistant are D-waves.

Many anaesthetic agents impact upon IONM signal quality. This interaction depends on the specific agent and the type of monitoring in use. Appropriate drug selection and administration, and minimisation of physiological variation, can improve patient safety by optimising evoked potential signals (Soghomonyan et al. 2014). In most neurologically intact patients, adequate evoked responses can be obtained with a balanced anaesthetic regimen. Steady infusion rates and stable concentrations of inhalational agents are preferred. Bolus dosing and other variations may impact signal quality and mimic surgical trauma (Lotto, Banoub, and Schubert 2004) (Banoub, Tetzlaff, and Schubert 2003).

Depth of anaesthesia monitoring

During total intravenous anaesthesia (TIVA), which has become the standard of care in neuroanaesthesia, the risk of awareness under general anaesthesia (AAGA) is increased. In order to mitigate this, depth of anaesthesia (DOA) monitoring is instituted, often alongside conventional EEG. Bispectral Index (BIS) is the most common processed EEG monitor but has important limitations (Musizza and Ribaric 2010). It is important to note that the stimulation of MEPs can lead to a falsely high BIS reading (suggesting that the patient is less deeply anaesthetised than they are), whilst reduced cerebral perfusion can lead to a falsely low reading (suggesting that the patient is in a very deep plane of anaesthesia, when they are not). Cerebral oxygenation monitoring with near infrared spectroscopy (NIRS) detects changes in oxygenation and may be helpful in clarifying the latter (Tobias 2008). When in doubt, discuss the EEG with the neurophysiologist in order to accurately deduce the depth of anaesthesia.

Controversies

Since there are no universal guidelines for its use, there is a great deal of variation in how IONM is used in practice. A few regional guidelines recommend certain modalities of monitoring as standard practice (Macdonald et al. 2013) (Dionigi et al. 2013). Often the methods used are

dependent on local experience and expertise (Jameson, Janik, and Sloan 2007).

Many neurosurgical procedures have a very low incidence of severe postoperative neurological deficits. This low event rate makes the benefit of IONM difficult to prove in practice, particularly as no randomised controlled trials of IONM versus no IONM would receive ethical approval. This is one reason why the uptake of IONM has been primarily driven by surgical preference, and why practice continues to evolve in an ad-hoc fashion (Sala 2010).

Management of signal change

Reliable interpretation of IONM signals requires the combined experience and knowledge of surgeons, anaesthetists and neurophysiologists (Kim et al. 2013). Communication between these team members is imperative for the successful application of monitoring (Stecker 2012). Signal changes must be communicated to the rest of the operating team and responded to quickly in order to prevent injury (Stecker 2012).

There is currently no consensus as to what degree of waveform attenuation, or IONM signal change, is significant; this is typically tailored to each patient according to the experience of the neurophysiologist. In one large case series, patients with either complete loss of or greater than 50% waveform attenuation of transcranial MEPs tended to display evidence of postoperative neurological deterioration (Rho, Rhim, and Kang 2016), and so this is used as a conventional alert threshold.

When encountered, neurophysiologic changes should be reconfirmed by another signal acquisition before a concerted team effort begins to elucidate and correct the cause. Surgery should be paused during this time unless at a critical stage. Depending on the monitoring modality in use, the cause may be elicited by determining the anatomical level, laterality and location of the change (focal or global). The causes of IONM signal change can be divided into five broad categories: surgical, pharmacological (e.g. anaesthetic agents), physiological (e.g. hypoxia, hypotension, hypothermia, anaemia), positional (e.g. extreme head position, peripheral nerve compression, spine flexion or extension), and technical (e.g. lead failure or dislodgement, electrical interference). In general, surgical, technical, and positional aetiologies result in focal changes, while anaesthesia and physiologic aetiologies tend to produce global effects on neuromonitoring. A structured and systematic approach to the diagnosis of signal attenuation is highly

desirable and may be facilitated by a checklist (Table 14-1). The whole team must then reach a consensus as to whether the surgery is to proceed as normal, be expedited or abandoned, or other additional steps be taken (e.g. wake-up testing or intra-operative neuro-imaging). Evidence-based protocols should be developed to deal with intra-operative changes in IONM and to validate these prospectively (Fehlings et al. 2010).

Table 14-1. "Pause for cause" checklist to be deployed in the event of a signal change during IONM. Adapted with permission (Wing-hay and Chun-kwong 2019)

Neurophysiologist	• Check electrodes and connections • Optimise impedance of electrodes • Exclude artefact and noise • Repeat tests as required • Assess pattern and timing of changes
Anaesthetist	• Ensure no pharmacological or physiological changes have occurred that may affect signal
Surgeon	• Pause surgery if safe to do so • Recall manoeuvres just before signal loss • Irrigate surgical site with warm saline and/or papaverine • Refer to neurophysiologist and anaesthetist's views on possible aetiology • Consider intra- or postoperative neuro-imaging as appropriate

The future

Guidance and education

As different intra-operative monitoring modalities have been shown to have different sensitivities and specificities, devising practice guidelines tailored to specific procedures in specific spinal or cranial procedures is a priority (Rattenni et al. 2015) (Fehlings et al. 2010). The International Society of Intraoperative Neurophysiology (ISIN) is one organisation to which surgeons, anaesthetists and physiologists look for such guidance. As techniques evolve, more sophisticated equipment may be required as the number of recording and stimulating channels, stimulation parameters and acquisition software increases in complexity.

Patient safety may be improved in the future by mandating modality- and procedure-specific certifications for neurophysiologists as their workload increases and diversifies; highly specialised modalities include corticobulbar MEP, lateral spread response, intra-operative blink reflex and laryngeal adductor reflex. Additionally, advanced accreditation might be considered in techniques such as trigeminal nerve SSEP, selective dorsal rhizotomy and the bulbocavernosus reflex.

Communication

Communication during neurosurgical procedures has always been challenging. With a large number of team members present in the operating theatre, the exchange of information in a clear, precise and adequate manner is easily compromised. Technology has the potential to improve accuracy and decision-making when multi-disciplinary insight is required to accomplish consistent and successful surgical outcomes. Automatic data sharing between neurophysiologist and neuro-anaesthetist could enable the former to interpret signals in the context of the prevailing anaesthetic and pharmacological conditions, whilst the latter could benefit from EEG data to inform their assessment of depth of anaesthesia. Surgeons would also benefit from such consolidated data, which could be made available on a separate screen or even displayed directly into the operating microscope.

Novel drugs

TIVA is currently the standard of care in neuroanaesthesia where IONM is to be used. The search continues for the ideal hypnotic agent which might confer anaesthesia whilst preserving neurological function. Modulation of the brainstem reticular formation and/or thalamus – either electrically or magnetically – may also one day achieve the same effect.

Advancing technologies

Alternatives to awake patient monitoring is needed to improve patient comfort and safety. Patients undergoing awake craniotomies are prone to increased levels of anxiety and stress during these procedures. After-discharges induced by monopolar or bipolar stimulation can evolve to produce clinical seizures and jeopardise complete resection. Moreover, complete pain management in these procedures is difficult, and hence it is not suitable for all patients.

Artificial intelligence

The advent of artificial intelligence (AI) has the potential to revolutionise the way IONM is practised. AI is composed of core subfields, each providing potential solutions to various clinical problems. Machine learning, artificial neural networks and computer vision will allow AI to improve intra-operative monitoring efficacy by predicting the potential risk of neurological injury faster and with greater accuracy than conventional human methods. In the future, AI may be used in conjunction with augmented reality to generate neurophysiological superimposed images under the operating microscope to enable surgeons to recognise anatomic and neural structures more distinctly.

References

Banoub, M., J. E. Tetzlaff, and A. Schubert. 2003. "Pharmacologic and physiologic influences affecting sensory evoked potentials: implications for perioperative monitoring." *Anesthesiology* 99 (3):716-37.

Dionigi, G., F. Y. Chiang, H. Dralle, L. Boni, S. Rausei, F. Rovera, E. Piantanida, A. Mangano, M. Barczynski, G. W. Randolph, R. Dionigi, and C. Ulmer. 2013. "Safety of neural monitoring in thyroid surgery." *International Journal Of Surgery* 11 Suppl 1:S120-6.

Fehlings, M. G., D. S. Brodke, D. C. Norvell, and J. R. Dettori. 2010. "The evidence for intraoperative neurophysiological monitoring in spine surgery: does it make a difference?" *Spine* 35 (9 Suppl):S37-46.

Jameson, L. C., D. J. Janik, and T. B. Sloan. 2007. "Electrophysiologic monitoring in neurosurgery." *Anesthesiology Clinics* 25 (3):605-30, x.

Kim, S. M., S. H. Kim, D. W. Seo, and K. W. Lee. 2013. "Intraoperative neurophysiologic monitoring: basic principles and recent update." *Journal of Korean Medical Science* 28 (9):1261-9.

Legatt, A. D., R. G. Emerson, C. M. Epstein, D. B. MacDonald, V. Deletis, R. J. Bravo, and J. R. Lopez. 2016. "ACNS Guideline: Transcranial Electrical Stimulation Motor Evoked Potential Monitoring." *Journal of Clinical Neurophysiology* 33 (1):42-50.

Lotto, M. L., M. Banoub, and A. Schubert. 2004. "Effects of anesthetic agents and physiologic changes on intraoperative motor evoked potentials." *Journal of Neurosurgical Anesthesiology* 16 (1):32-42.

Macdonald, D. B., S. Skinner, J. Shils, C. Yingling, and Monitoring American Society of Neurophysiological. 2013. "Intraoperative motor evoked potential monitoring - a position statement by the American

Society of Neurophysiological Monitoring." *Clinical Neurophysiology* 124 (12):2291-316.
Musizza, B., and S. Ribaric. 2010. "Monitoring the depth of anaesthesia." *Sensors* 10 (12):10896-935.
Nuwer, M. R., R. G. Emerson, G. Galloway, A. D. Legatt, J. Lopez, R. Minahan, T. Yamada, D. S. Goodin, C. Armon, V. Chaudhry, G. S. Gronseth, C. L. Harden, Neuromuscular American Association of, and Medicine Electrodiagnostic. 2012. "Evidence-based guideline update: intraoperative spinal monitoring with somatosensory and transcranial electrical motor evoked potentials*." *Journal of Clinical Neurophysiology* 29 (1):101-8.
Rattenni, R. N., T. Cheriyan, A. Lee, J. A. Bendo, T. J. Errico, and J. E. Goldstein. 2015. "Intraoperative Spinal Cord and Nerve Root Monitoring: A Hospital Survey and Review." *Bulletin of the Hospital for Joint Disease* 73 (1):25-36.
Rho, Y. J., S. C. Rhim, and J. K. Kang. 2016. "Is intraoperative neurophysiological monitoring valuable predicting postoperative neurological recovery?" *Spinal Cord* 54 (12):1121-1126.
Sala, F. 2010. "Intraoperative neurophysiology is here to stay." *Childs Nervous System* 26 (4):413-7.
Sala, F., A. Coppola, V. Tramontano, M. Babini, and G. Pinna. 2015. "Intraoperative neurophysiological monitoring for the resection of brain tumors in pediatric patients." *Journal of Neurosurgical Sciences* 59 (4):373-82.
Sala, F., and C. Di Rocco. 2015. "Intraoperative neurophysiological monitoring in neurosurgery: moving the debate from evidence and cost-effectiveness to education and training." *World Neurosurgery* 83 (1):32-4.
Soghomonyan, S., K. R. Moran, G. S. Sandhu, and S. D. Bergese. 2014. "Anesthesia and evoked responses in neurosurgery." *Frontiers in Pharmacology* 5:74.
Stecker, M. M. 2012. "A review of intraoperative monitoring for spinal surgery." *Surgical neurology international* 3 (Suppl 3):S174-87.
Tobias, J. D. 2008. "Cerebral oximetry monitoring with near infrared spectroscopy detects alterations in oxygenation before pulse oximetry." *Journal of Intensive Care Medicine* 23 (6):384-8.
Wing-hay, H.Y., and E.C. Chun-kwong. 2019. "Introduction to Intraoperative Neurophysiological Monitoring for Anaesthetists." World Federation Of Societies of Anaesthesiologists, accessed 21st April 2019. www.wfsahq.org.