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Invited review

Intraoperative neurophysiological monitoring of the spinal cord during spinal cord and spine surgery: A review focus on the corticospinal tracts

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Abstract

Recent advances in technology and the refinement of neurophysiological methodologies are significantly changing intraoperative neurophysiological monitoring (IOM) of the spinal cord. This review will summarize the latest achievements in the monitoring of the spinal cord during spine and spinal cord surgeries. This overview is based on an extensive review of the literature and the authors' personal experience. Landmark articles and neurophysiological techniques have been briefly reported to contextualize the development of new techniques. This background is extended to describe the methodological approach to intraoperatively elicit and record spinal D wave and muscle motor evoked potentials (muscle MEPs). The clinical application of spinal D wave and muscle MEP recordings is critically reviewed (especially in the field of Neurosurgery) and new developments such as mapping of the dorsal columns and the corticospinal tracts are presented. In the past decade, motor evoked potential recording following transcranial electrical stimulation has emerged as a reliable technique to intraoperatively assess the functional integrity of the motor pathways. Criteria based on the absence/presence of potentials, their morphology and threshold-related parameters have been proposed for muscle MEPs. While the debate remains open, it appears that different criteria may be applied for different procedures according to the expected surgery-related morbidity and the ultimate goal of the surgeon (e.g. total tumor removal versus complete absence of transitory or permanent neurological deficits). On the other hand, D wave changes – when recordable – have proven to be the strongest predictors of maintained corticospinal tract integrity (and therefore, of motor function/recovery). Combining the use of muscle MEPs with D wave recordings provides the most comprehensive approach for assessing the functional integrity of the spinal cord motor tracts during surgery for intramedullary spinal cord tumors. However, muscle MEPs may suffice to assess motor pathways during other spinal procedures and in cases where the pathophysiology of spinal cord injury is purely ischemic. Finally, while MEPs are now considered the gold standard for monitoring the motor pathways, SEPs continue to retain value as they provide specificity for assessing the integrity of the dorsal column. However, we believe SEPs should not be used exclusively – or as an alternative to motor evoked potentials – during spine surgery, but rather as a complementary method in combination with MEPs. For intramedullary spinal tumor resection, SEPs should not be used exclusively without MEPs.

Keywords: Intraoperative monitoring; Spinal cord surgery; Spine surgery; Motor evoked potentials; D wave

1. Introduction

Recent advances in technology and neurophysiological methodologies are significantly changing intraoperative neurophysiological monitoring (IOM) of the spinal cord.

Approximately 30 years have passed since somatosensory evoked potentials (SEPs) were first used to monitor the spinal cord during surgical correction for scoliosis (Nash et al., 1977; Engler et al., 1978). Early enthusiasm was stemmed by the presence of serious motor deficits despite preserved SEPs. Thus, their capacity to monitor the spinal cord motor tracts began to be questioned.

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Lesser et al. presented the first report in the literature of a patient who suffered post-operative paraplegia despite SEP preservation (Lesser et al., 1986). This extensively-cited paper combines data dealing with this phenomenon from 6 different centers. A review of the original papers, which Lesser's work is based on, shows that at least one patient (from Ginsburg et al., 1985) had what he believed were post-operatively preserved SEP recordings even while the patient was paraplegic. Following Lesser et al., reports in the literature continued to show the presence of preserved SEPs at the end of surgery in patients who suffered post-operative paraplegia (Zornow et al., 1990; Minahan et al., 2001; Jones et al., 2003; Pelosi et al., 1999). Most of the patients from these four studies had anterior spinal artery syndrome, which only affected the vascular territory of the anterolateral column of the spinal cord. This is a primary factor that influences the preservation of the dorsal column, which is a major contributor in the generation of SEPs. Furthermore, preserved SEPs, coupled with the loss of muscle motor evoked potentials (muscle MEPs), have been documented in surgery for intracranial blood vessels (Neuloh and Schramm, 2002; Szelenyi et al., 2003).

Lesions to the corticospinal tracts (CTs) or dorsal columns can inadvertently occur as well during surgery for intramedullary spinal cord pathology. If a lesion occurs when approaching the intramedullary tumor during the initial dorsal myelotomy, SEPs can completely disappear, a drawback that compromises the use of SEPs as the only neurophysiological monitoring method for this type of surgery (Kalkman et al., 1994; Deletis, 1999).

These limitations supported the opinions of some neurosurgeons who had come to believe that SEPs were useless during surgery of the spinal cord. Although that statement sounded rather extreme, it was worthy of notice given that the recording of SEPs was the only available monitoring technique at that time. In the last 10 years, however, the development of specific methods for monitoring the functional integrity of the CTs has opened a new field in the monitoring of the motor tracts during spine and spinal cord surgery. Two specific methods are: (a) Recordings of the D wave from the spinal cord, and (b) Recordings of motor evoked potentials from the limb muscles. The combined use of these techniques has become useful in preventing surgically induced injury to the spinal cord and in predicting post-operative motor outcome (Kothbauer et al., 1997, 1998; MacDonald and Janusz, 2002). Today, methods for monitoring the dorsal and the lateral columns (CT) of the spinal cord are so refined that each long tract can be monitored individually, with changes correlating highly with post-surgical neurological outcome.

It should be mentioned that the terminology "false negative SEPs" is often inappropriately used to indicate the occurrence of a post-operative motor deficit in spite of unchanged intraoperative SEPs. A SEP result should be labeled as "false negative" only when post-operative sensory deficits occur and were not predicted by intraoperative SEP changes. Similarly, a MEP result should be labeled as "false negative" if the patient wakes up with a new or worsened motor deficit in spite of intraoperatively unchanged MEPs. This review will summarize the latest achievements in the monitoring of the spinal cord functional integrity during surgery of the spine and spinal cord, as well as the introduction of further developments in this field. This review is written by a clinical neurophysiologist (VD) and a neurosurgeon (FS) in order to give readers a balanced view of the role that intraoperative monitoring plays in the prevention and documentation of intraoperative injury to the spinal cord.

2. A brief history of intraoperative monitoring (IOM) of the spinal cord

Because of the previously mentioned disadvantages of using SEPs as the only monitoring method during surgery of the spine and spinal cord, a couple of different methods have been developed with the hope of better evaluating the functional integrity of the spinal cord's long pathways. In the course of developing the clinical use of these methods, it has been shown that most of them cannot evaluate CT functional integrity because they are not specific to the fast neurons in the CT, which are essential elements for execution of precise voluntary movements.

2.1. Spinal cord-to-spinal cord technique

In this method, the spinal cord is stimulated with an epidural catheter-type electrode, then the elicited compound potentials are recorded over the spinal cord (Tamaki et al., 1985, 1986). Stimulation can be performed cranially and recorded caudally or vice versa. Due to the different conduction properties (velocities) of the spinal cord pathways, the recorded potentials take the form of two distinct waves. The recorded potentials are very robust and most likely represent the combined activity of the dorsal columns (DCs), the CTs, and other tracts of the spinal cord. It has been claimed that one of these two waves belonged to the DC and the other to the CT. Unfortunately, there is not enough evidence to verify this statement. Koyanagi et al., could not find a clear correlation between results using this method and the clinical outcome of 20 patients who underwent surgery for intramedullary spinal cord tumors (Koyanagi et al., 1993). This monitoring method has been largely abandoned today, but it retains some value when there is severe preexisting neuropathology, or in research settings, when determination of the extent of conduction may be important.

2.2. Spinal cord-to-peripheral nerve ("Neurogenic MEPs")

On the basis of Machida's work (Machida et al., 1985), Owen and colleagues introduced a method that electrically stimulates the spinal cord with trans-laminally-placed electrodes in order to elicit potentials that are then recorded from the peripheral nerves (Owen et al., 1991). They named these potentials neurogenic MEPs, claiming that they represented the activity of the spinal cord's motor pathways. However, following a decade of analysis by intraoperative neuromonitoring teams in the USA and Europe, increasing evidence is beginning to question this belief. By using a collision technique, Toleikis et al., have shown that neurogenic MEPs are not potentials recorded from the motor pathways, but instead represent antidromic potentials from the electrically stimulated DC axons (Toleikis et al., 2000). Additionally, Minahan and colleagues described two paraplegic patients whose neurogenic MEPs (as well as SEPs) were preserved at the end of surgery (Minahan et al., 2001). Using Toleikis' collision technique, Pereon et al., published data showing that the second polyphasic component of a neurogenic MEP did not disappear after colliding with peripheral nerve antidromic activity. The first slow component disappeared when the collision occurred at the spinal cord level (Pereon et al., 2002). However, this experiment did not prove that the second polyphasic component of neurogenic MEPs originated from CT activity. Furthermore, because of its low amplitude, it is not always possible to distinguish the second polyphasic component from background noise. So far, strong clinical and neurophysiological evidence indicates that the slow (first) component of the neurogenic MEP is antidromic activity of the DC and should be used only as a method for monitoring the functional integrity of the dorsal column and not for monitoring the CT (Deletis, 2001e). This evidence is of utmost importance considering that, in a recent survey on the use of MEP monitoring, 15 out of 39 centres, mainly in USA, still described the use of spinal cord stimulation with recording of neurogenic (or myogenic) MEPs as their preferred technique to elicit MEPs during spinal cord monitoring (Legatt, 2002, Table 5).

2.3. Spinal cord-to-muscle ("Myogenic MEPs")

Machida described a monitoring method whereby compound muscle action potentials (CMAPs) were recorded following electrical stimulation of the spinal cord via a catheter electrode (Machida et al., 1985). Taylor et al. modified this method by using two stimuli, and recommended an optimal inter-stimulus interval of 2 ms, to facilitate the elicitation of CMAPs. In the literature, this method has been referred to as myogenic MEPs (Taylor et al., 1993). It is still unknown whether or not myogenic MEPs result from CT activity.

2.4. Spinal cord-to-scalp

This method uses stimulation of the spinal cord (Berić et al., 1986; North et al., 1991), or cauda equina (Luders et al., 1982), to intraoperatively record SEPs from the scalp. SEPs obtained by this method are generally of high amplitude and can be easily used for monitoring. However, for reasons still unknown, its use has not been widely accepted. SEPs obtained by this method have higher amplitudes than peripheral-nerve-elicited SEPs because the entire afferent input from the lower limbs is activated. It is interesting that most of the authors who used the spinal cord stimulation method, also recorded an early potential, which appeared before cortical SEPs (North et al., 1991; Drenger et al., 1992). Partanen et al. claimed that this early potential was antidromic activity of the CT mixed with far-field subcortical potentials from the dorsal column nuclei (Partanen et al., 2000). They based their conclusion on the partial sensitivity that these potentials exhibited in the presence of isoflorane – an inhaled anesthetic known to be a very potent agent for blocking synaptic transmission. The jury remains out on whether these potentials really represent antidromic CT activities.

As a note, Humphrey showed in an animal study that if CT of the spinal cord is electrically stimulated, its antidromic activity can be recorded from the cerebral cortex. He named this synchronized antidromic activity the A-wave (Humphrey, 1968).

3. Current developments

3.1. MEPs recordings following transcranial (or direct) electrical stimulation of the brain

Penfield and Boldrey showed that limb and face movements could be elicited by applying a train of stimuli of several seconds at a frequency between 50 and 60 Hz over the exposed human motor cortex (Penfield and Boldrey, 1937). This method has been widely used for the last half century to determine the location of the motor cortex in anesthetized patients during open brain surgery as well as the location of language cortical areas during craniotomy while patients were awake.

Because it would be necessary to open the skull in order to stimulate the motor cortex, and also because such stimulation has been shown to induce a high incidence of seizures (in up to 30% of patients), this methodology is not suitable for monitoring the spinal cord's motor tracts.

3.2. Single pulse stimulating technique

In the 1980s, Merton and Morton discovered that a high-voltage single electrical stimulus applied over the skull could activate the motor cortex and consequently generate MEPs, which could be easily recorded from the limb muscles (Merton and Morton, 1980a,b). The method was first tried on conscious patients, and later, in the operating room with anesthetized patients (Fig. 1). The use of this method in anesthetized patients became problematic because anesthetics impaired the motor cortex's ability to generate multiple descending volleys (in the form of the D and multiple I waves) after a single electric stimulus applied over the skull. These multiple descending volleys are one of the prerequisites for generating muscle MEPs. Furthermore anesthetics depress the excitability of the entire spinal cord, including alpha-motoneuron pools.

For more than a decade, this remained an insurmountable obstacle when using the single stimulus method to elicit muscle MEPs. The single stimulus method can generate muscle MEPs only if the patient is not deeply anesthetized or in cases where a special combination of intravenous anesthetics for general anesthesia is used (total venous anesthesia). Even when such a combination of anesthetics is used, muscle MEPs may not be successfully generated in all patients (Zentner, 1989).

Because of this, the single-pulse stimulating technique has been almost exclusively used to elicit intraoperative D and I waves which are then recorded from the epi- or subdural space of the spinal cord (Boyd et al., 1986; Katayama et al., 1988; Burke et al., 1992; Deletis, 1993).

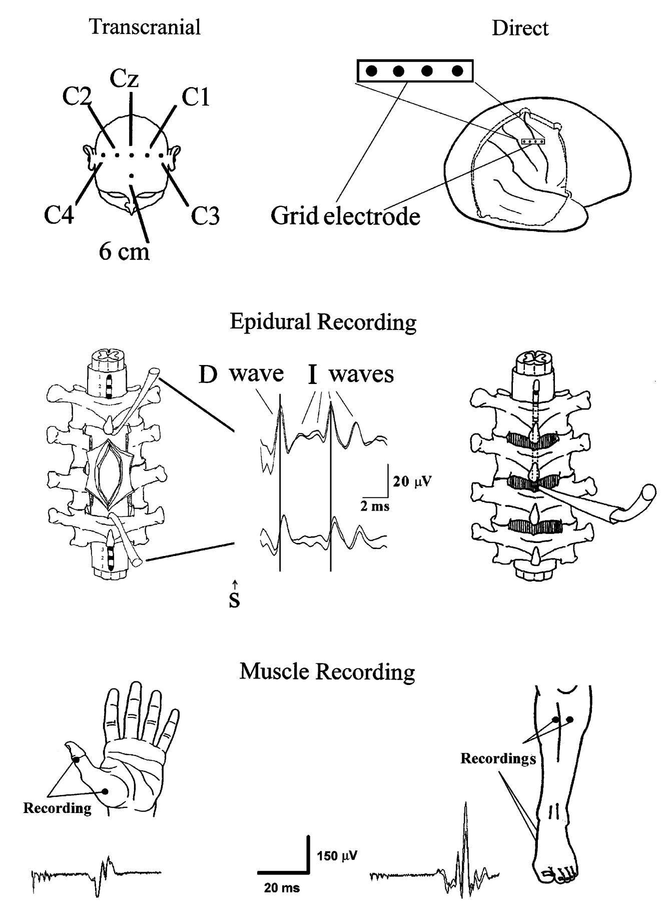

Fig. 1. Schematic drawing of intraoperative methodology for eliciting and recording motor evoked potentials from the spinal cord and limb muscles. *Top*: Schematic illustration of electrode positions for transcranial and direct electrical stimulation of the motor cortex according to the International 10-20 EEG system. *Middle*: Schematic diagram of the positions of the catheter electrodes (each with three recording surfaces) placed cranial to the tumor (control electrode) and caudal to the tumor to monitor the incoming signal passing through the site of surgery. In the middle are D and I waves recorded rostral and caudal to the tumor site. Please note the peak latency difference between cranial and caudal recordings of the D and I waves is marked with vertical lines. *Bottom*: Recording of muscle motor evoked potentials from the thenar, tibialis anterior and abductor hallucis muscles after eliciting them with a short train of electrical pulses applied transcranially (Modified from Deletis and Sala, 2001c).

3.3. Multipulse stimulating technique

By applying a short train of 5–7 electrical pulses over the scalp or exposed motor cortex, the alpha-motoneurons receive multiple descending volleys with enough potency to reach their firing thresholds and, consequently, generate muscle MEPs (Taniguchi et al., 1993; Pechstein et al., 1996) (Fig. 1). Furthermore, it has been shown that three or more stimuli applied over the scalp of anesthetized patients can facilitate the generation of I waves (Deletis et al., 2001b). Consequently, when given separately, the three stimuli that individually generate D waves only can actually generate four descending volleys (three D and one I wave) if given in a short-train. In many patients, this phenomenon increases the potency of multiple stimuli applied over the motor cortex for generating muscle MEPs. It is interesting that this phenomenon had been previously recorded by Phillips and Porter in an animal study but was not recognized until recently (Philips and Porter, 1964; Deletis et al., 2001b).

Due to their relative desynchronization, I wave activity is three times greater than epidural recordings indicate (Amassian and Deletis, 1999). This emphasizes the importance of the multiple descending volleys, ensuring that the alpha-motoneurons reach their firing thresholds.

In an animal study, killed-end potentials were used to extrapolate and compare amplitudes of D and I waves recorded in humans (Amassian and Deletis, 1999).

3.4. Methodological aspect for eliciting and recording D wave and muscle MEPs

A single electrical pulse delivered either transcranially or over the exposed motor cortex is adequate for eliciting a D wave. So far, current available FDA-approved stimulators have a constant voltage output, even though some of them can also read delivered-current intensity in mA. Theoretically, constant-current stimulators used for transcranial electrical stimulation (TES) are a better technical solution because current delivered to the brain does not depend on the impedance of stimulating electrodes, and this is important only when impedance changes during operation.

A review of the literature shows that most of the published papers about MEPs use constant-voltage stimulators (Boyd et al., 1986; Burke et al., 1992, 2000; Hausmann et al., 2002; Jones et al., 1996, 2003). Satisfactory results for eliciting MEPs during everyday practice can be achieved with constant-voltage stimulators. However when finding the right TES parameters becomes critical, as may be the case in a research study or on threshold measurements for MEPs, the constant-voltage stimulators that are currently on the market may provide misleading results (Journee et al., 2003).

In addition to Digitimer (Welwyn Garden City, UK), other companies such as Cadwell (Cadwell Lab Inc, Kennewick, WA, USA), Axon (Axon Inc. Hauppauge, NY, USA), and Nicolet (Nicolet Co., Madison, WI, USA) have recently obtained FDA clearance to use their transcranial electrical simulators as part of their intraoperative monitoring systems. Inomed (Inomed, Tenningen, Germany) has also introduced a transcranial stimulator that does not yet have FDA approval.

A short train of stimuli is preferable when eliciting muscle MEPs in anesthetized patients. This will generate multiple descending volleys which are carried by the fast CT neurons, the critical elements for the sufficient depolarization of the spinal cord's alpha-motoneurons. There is no agreement on the optimal parameters of the short train of stimuli, which are: (a) The number of pulses in the train. (b) The individual pulse duration. (c) The inter-stimulus interval. (d) The train repetition rate.

The physiology of the D and I waves in anesthetized patients and their relationship to muscle MEPs have been discussed and documented in three papers dealing with these type of problems (Deletis et al., 2001a,b; Novak et al., 2004). These papers can be summarized as follows:

a. The most efficient duration of the stimulus in the train is 0.5 ms because this longer duration allows for the quicker recovery of each consecutive D wave amplitude. The disadvantage in using a longer individual pulse duration in the train is that it uses more charge (Bartley et al., 2002).
b. The inter stimulus interval (ISI) in the train of stimuli is dependent on the intensity of the stimulus. With stronger intensities shorter ISIs can be used (but not shorter than 2 ms) (Novak et al., 2004). The papers find, however, that the optimal ISI, regardless of intensity, is 4 ms. This parameter can be applied in patients where a single pulse TES can generate a single D wave (without I waves), which is the case with most moderately anesthetized patients. Therefore, theoretically, the optimal parameters for a train of stimuli should be established only when the descending volleys (which are carried by the fast neurons of the CTs) can be read by recordings from epi- (or sub-) dural electrodes placed over the spinal cord (before volleys reach the alpha-motoneuron pool). In everyday practice, it is not always possible to simultaneously record D and I waves and muscle MEPs. But by doing so in a large group of patients, we discovered that a single stimulus of medium intensity can elicit one or more I waves in addition to eliciting the D wave in a minority of patients (Deletis et al., 2001b). Therefore, the optimal stimulation parameters recommended earlier should be applied in order to successfully elicit muscle MEPs.
c. Train repetition rate (numbers of trains per one second) is an important variable, although we are not aware of a single peer-reviewed paper dealing with this problem. In our experience, the faster the train repetition rate the higher the MEP amplitude (Deletis, 2002b). A train repetition rate of 2 Hz is suggested as optimal. More data are needed on this phenomenon in order to pinpoint optimal parameters.

For TES the choice of the electrode montage on the scalp remains the focus of some debate. Some combinations are mentioned in the literature (Szelenyi et al., 2007b) and their advantages in eliciting muscle MEPs have been discussed. (C1, C2, Cz [or 1 cm behind Cz], C3, C4, and 6 cm in front of Cz.) The combination of stimulating points should be tailored for each patient in order to optimize TES and avoid generalized twitches, especially in the shoulder, neck and torso muscles, which might interfere with the surgical procedures. Therefore it is recommended to attach electrodes at all stimulating points over the head, as shown in Fig. 1, before surgery starts, and choose the optimal combination for each patient. This might be a critical point in the methodology because in some patients a combination of Cz (+) and 6 in front of Cz (−), for instance, can elicit responses only in the lower extremities without disturbing twitches in other parts of the body (Deletis, 2002b). Some authors prefer C3 (C4)/versus Cz (Burke et al., 1992, 2000) or C3/C4 (Jones et al., 1993,1996). For TES, the anode (+) is an active (stimulating) electrode which should be positioned over the specific motor cortex areas to be stimulated. If one would like to elicit MEPs in the right hand, C3 (+) versus C4 (−) should be used. For the left hand muscles, the polarity of the stimulating electrode should be reversed. Burke's group prefers to use C3 or C4 (+) versus Cz (−) for hand stimulation, and Cz (+) versus C3 (−) or C4 (−) for the motor leg area. It is important to mention that this selectivity in the stimulation of the smaller areas of the motor cortex (or part of the CT originated from it) can be achieved only with a rather low stimulus intensity. When transcranially applied stimuli reach a certain intensity, both the cathode and the anode become the stimulating electrodes, while the current passing between them stimulates the CT deep within the brain, activating almost all descending fibers (Rothwell et al., 1994). On the basis of the D wave latency measurements, it has been postulated that there are three favorable points which are susceptible to CT depolarization: cortex/subcortex (weak electrical stimulation), internal capsule (moderate electrical stimulation), and brainstem/foramen magnum (very strong electrical stimulation). The ability to selectively stimulate is only possible at the level of the cortex (subcortex). Therefore, only relatively weak electrical stimuli to the cortex are selective, and they activate only a small portion of the CT fibers (e.g. activating only one extremity) or predominantly one CT (Rothwell et al., 1994).

In order to be selective during stimulation, authors from Nihon University (Tokyo) suggested the placement of stimulating electrodes through the skull bur hole(s) (Katayama et al., 1988, 1993). However, this approach is considered by many people in the field to be too invasive for routine IOM of the spinal cord.

The type of electrode used for TES varies among authors and these can be categorized in three groups: (a) Surface electrodes, usually EEG cup electrodes fixed to the scalp by collodion. (b) EEG needle electrodes. (c) Specially-modified needle electrodes in the shape of a cork screw (CS electrode, Nicolet Biomedical, Madison, WI). Cork screw electrodes are the most suitable for TES during IOM because they have low impedance and they cannot be easily displaced or detached from the scalp, with the exception of their use in babies in whom the fontanelles still exist. Since cork screw or needle electrodes can potentially penetrate the fontanel during placement, the use of EEG cup electrodes is recommended.

For D wave recordings, different types of electrodes are used for insertion in either the spinal epidural or subdural space (Katayama, Tamaki et al., 1985; Boyd et al., 1986; Burke et al., 2000; Deletis et al., 2001a). These types of electrodes produce D wave amplitudes of up to 80 μV in the cervical region during monitoring and approximately more than half of this value in the upper thoracic region, with a further drop in the lumbar region of the spinal cord. It is important to mention that all electrodes used for D wave recordings must have low impedance in order to avoid stimulus artifact caused by the strong current applied over the scalp. This is especially important when recording over the high cervical spinal cord. The distance between the electrode's recording surfaces should be at least 3 cm apart in order to obtain the optimal amplitudes (similar to the monopolar recordings). As it usually produces large artifacts, the needle (reference electrode) placed in the adjacent muscle should not be used.

When monitoring surgery for the high cervical spinal cord, the recording epidural electrode should be placed over the low cervical spinal cord. For monitoring the mid or lower cervical spinal cord, placement in the high thoracic spinal epidural space is recommended in order to avoid interfering with the surgery (the latter will not monitor the CT tracts for the upper extremities). However, according to previous experience, it is extremely rare to produce an ultra-selective lesion of the CT for the upper but not for the lower extremities during surgery in this region. This is due to the fact that the CTs for upper and lower extremities in the cervical spinal cord are in such a close proximity from each other.

Muscle MEPs can be recorded either via surface or EEG needle electrodes inserted in the belly muscle. Both types of electrodes give high amplitude muscle MEPs, usually up to 100 μV or more. Because of their low impedance and safety concerning sterilization, we prefer disposable EEG needle electrodes.

The selection of appropriate muscles to record from is an important issue in the monitoring of muscle MEPs. In certain patients with severe paresis, choosing non-optimal muscles can result in non-monitorable patients. The small hand muscles (e.g. abductor pollicis brevis or first dorsal interosseus muscle) are some of the optimal muscles to monitor the CT for the upper extremities. But the long forearm flexors or even the forearm extensors have been shown to be good alternatives (Taniguchi et al., 1993). The spinal motoneurons for these muscle groups have rich CT innervation and are therefore suitable for monitoring the functional integrity of the CT. This is not the case with the proximal muscles of the arm or of the shoulder (biceps, triceps, or deltoid muscles).

For the lower extremities, the abductor hallucis (AH) is the optimal muscle because of its dominant CT innervation. In animal experiments, it has been shown that following CT stimulation the highest amplitude of the EPSP has been found in the alpha-motoneuron pools for the lower extremity muscles (small and long flexors of the foot) (Jankowska et al., 1975). The tibial anterior muscle (TA) is an alternative to the AH. Our standard electrode montages for monitoring muscle MEPs are the AH and TA for the lower and the APB and forearm flexors or extensors for the upper extremities. Increasing the number of monitored muscles does not give us tremendous advantages. Because of the overlap of myotomal innervation, it is unlikely that muscle MEPs can provide adequate information during surgery where a root lesion occurs.

The normal variation in D wave amplitude, in single D wave recordings, is 10%. This is considered to be within normal physiological variations (Burke et al., 1995). The same group reported that more than a 20% change in averaged D wave recordings should be considered a warning sign (Burke and Hicks, 1998). In spinal cord surgery, a 50% decrement of the D wave amplitude has been recommended (Kothbauer et al., 1998; Sala et al., 2006) (see the next paragraph).

3.5. Monitoring of the spinal cord motor pathways by combination of muscle MEPs and D waves

Muscle MEP monitoring seems to be an adequate method for monitoring the functional integrity of the CTs during most spine surgeries (Pelosi et al., 2002; DiCindio et al., 2003; Deletis and Sala, 2004). This is not true for spinal cord surgery, and more specifically, not true for intramedullary spinal cord tumor surgery (IMSCT). In well documented studies on more than 100 IMSCT surgeries, it has been shown that a preserved D wave up to 50% of the original amplitude, with a complete loss of muscle MEPs, will result in only transient paraplegia (Kothbauer et al., 1997, 1998; Sala et al., 2006).

These patients woke up with severe motor deficits after surgery (a few even paraplegic and flaccid), but all recovered completely within a few hours to a few weeks (Deletis and Kothbauer, 1998; Sala et al., 2006). This data is quite opposite to the position taken by Calancie et al. that even slight changes in the threshold for eliciting muscle MEPs should be a warning sign of an imminent CT lesion (Calancie et al., 1998). If IMSCT surgery is only monitored with muscle MEPs, without the D wave, then significant changes in the threshold for eliciting muscle MEPs should not necessarily indicate injury to the CTs. This is due to the fact that we do not have specific information about the functional integrity of the fast neurons of the CT. Therefore any warning that the CT is in imminent jeopardy, based on an increase in the threshold for eliciting muscle MEPs, may be inaccurate. Furthermore, not only can an increase in the threshold for eliciting muscle MEPs be tolerated, but even the complete disappearance of muscle MEPs is acceptable, if monitoring for intramedullary tumors is done with both D waves and muscle MEPs (Kothbauer et al., 1997, 1998; Sala et al., 2006). This scenario has proved to correlate with severe post-operative motor deficits that invariably recover over time because the CT is preserved. When IMSCT surgery is performed with a very precise instrument, such as the Nd/YAG Contact Laser (SLT, Montgomeryville, PA), a lesion to other structures than the fast axons of the CT might occur without causing major injury to the CT (Jallo et al. 2002a, 2002b). A preserved D wave at the end of surgery (at least 50% of its original amplitude) is an assurance that the fast neurons of the CT tracts responsible for fine voluntary movement remain intact (Fig. 2). Preservation of the D wave becomes a critical factor, for as long as it is present, the patient's fine voluntary movement will be preserved in the long run (Sala et al., 2006). Further evidence that D wave preservation during surgery is of utmost importance comes from the work of Yamamoto et al. and Fujiki et al. who showed that a decrement of more than 30% of D wave amplitude elicited by one hemisphere stimulation in supratentorial surgery inevitably resulted in a deep hemilateral motor deficit (Yamamoto et al., 2004; Fujiki et al., 2006). This 30% criteria, after stimulating one hemisphere, correlates well with the 50% criteria used in spinal cord monitoring, where both hemispheres are activated.

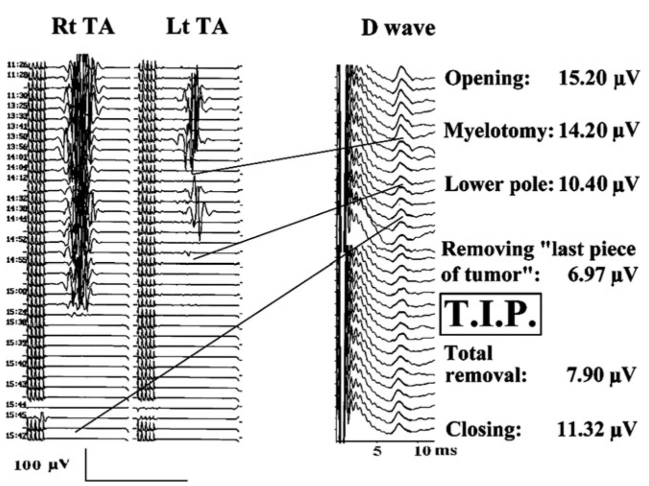

Fig. 2. During surgery for a Th4–Th6 ependymoma, the progressive loss of the left (time 14:55) and right (time 15:38) tibialis anterior muscles (left panel) was observed. Meanwhile, D wave amplitude decreased by approximately 30% of initial values and surgery was not stopped. However, at time 16:00, when the attempt was made to remove the last piece of tumor adherent to the left anterolateral corticospinal tract, we observed a dramatic drop of D wave amplitude and surgery was transiently stopped. Corrective measures were taken (T.I.P., see text for a details) and total tumor removal was finally achieved about 20 minutes later when the D wave amplitude recovered to 7.90 µV. At the closing D wave amplitude recover and it was 11.32 µV (14% drop from the opening baseline amplitude). Reprinted from Sala et al., 2004.

Patients who lose the D wave during spinal cord surgery usually become permanently paraplegic (Morota et al., 1997). Furthermore, in patients who are already paraplegic before surgery, D waves cannot be recorded caudal to the lesion of the spinal cord (Boyd et al., 1986).

This indicates how critical it is to simultaneously monitor the D wave and muscle MEPs during surgery for the spinal cord. Table 1 summarizes the correlation between neurophysiological signals during surgery for IMSCT and post-operative neurological outcome based on 150 surgeries for IMSCT performed in two surgical centers (Kothbauer et al., 1997, 1998; Sala et al., 2006).

When the D wave is not present before surgery for intramedullary spinal cord tumor (due to its extreme desynchronization), a 50% drop in muscle MEPs can still be tolerated. The basis for this approach lies in the fact that the D wave amplitude never becomes more than 50% diminished unless muscle MEPs are greatly attenuated (Kothbauer et al., 1997, 1998). Without the D wave, muscle MEPs should be carefully monitored. No more than 50% of muscle MEP amplitude drop should be tolerated as we do not know whether such occurrence correlates with transient or permanent paraplegia.

Whether or not we can perform TES in a patient with preexisting seizures continues to be a question of debate. Each of these patients should be individually assessed to ascertain the risk versus benefit. At least in supratentorial surgeries, during electrical stimulation of the brain there is evidence that the incidence of intraoperative seizures is not more frequent in a group of patients with a seizure versus patients without (Szelenyi et al., 2007a). Furthermore, there is no evidence that intraoperatively performed TES induces post-operative seizures or modifies the frequency of its appearance in patients with epilepsy. Relative contraindications to this include epilepsy, skull defects, elevated intracranial pressure, cardiac disease, cardiac pacemakers or other implanted biomedical devices (MacDonald, 2002). As mentioned earlier, only patients with deep motor deficits (deep para- or quadriparesis) or more profound neurological deficits (para- or quadriplegia) are not good candidates for muscle MEPs monitoring because it is highly likely that muscle MEPs cannot be elicited. DiCindio and colleagues showed that even in the patient with

Table 1
Principles of MEP interpretation (reproduced from Deletis, 1999)

D wave	Muscle MEP[a]	Motor status (postoperatively)
Unchanged or 30–50% decrease	Preserved	Unchanged
Unchanged or 30–50% decrease	Lost uni- or bilaterally	Transient motor deficit
>50% Decrease	Lost bilaterally	Long term motor deficit

[a] In the tibial anterior muscle(s).

cerebral palsy, muscle MEPs can be successfully monitored (DiCindio et al., 2003). In patients with a skull defect, TES can be performed successfully without jeopardizing the patient.

3.6. Disadvantages of D wave monitoring

(1) In about 20% of patients with IMSCT, or post-radiation myelopathy, the D wave is not present at the beginning of surgery even when muscle MEPs can be recorded. These findings are consistent with previous reports suggesting that radiation therapy seriously damages conductivity in the spinal cord's long tracts (Scisciolo et al., 1991). This phenomenon is probably due to the desynchronization of descending activity through the CT which the D wave reflects (Deletis and Kothbauer, 1998). Therefore, this activity cannot be recorded caudal to the lesion site (due to myelopathy or the presence of tumor). In this situation, when the D wave is absent at the beginning of surgery, the disappearance of muscle MEPs during surgery cannot be used to predict either permanent or transient lesions to the motor system primarily because in these patients specific information about CT is not obtainable.

(2) Another disadvantage of the D wave monitoring method is that it cannot be applied during surgery on the spinal cord caudal to the Th 10–11 spinal cord segments because there are not enough fast CT axons to generate a D wave below that level with sufficient amplitude for monitoring.

(3) A recent article by Ulkatan et al. questioned the use of D wave recordings during scoliosis surgery given a high percentage of false positive and negative data. Their explanation is that D wave amplitude decrements (in 4 patients out of 93) or increments (in 21 out of 93), result from a new spatial relationship between the epidural recording catheter and spinal cord after surgical correction of the scoliosis. Parallel changes in muscle MEPs or SEPs were not noted. Therefore the authors expressed concern about using the D wave bipolar recordings as a method to judge the functional integrity of the CTs during monitoring of this specific pathology (Ulkatan et al., 2006).

(4) According to a report by MacDonald et al., the simultaneous monitoring of D wave, muscle MEPs and SEPs during surgery for thoracoabdominal aneurysm revealed that in one patient SEPs could better detect spinal cord segmental gray matter ischemia than the D wave could. In other patients, muscle MEPs were more sensitive for the ventral gray matter of the spinal cord than SEPs (MacDonald, 2002).

(5) In the same paper the authors described false positive results during D wave monitoring due to scalp edema when using cork screw electrodes. In other papers the same phenomenon has been described during muscle MEP monitoring (MacDonald, 2006). In both instances, the authors used subcutaneous electrode for TES. It remains a question of interpretation whether these results belong to the category of real false positive data when the scalp edema can be ruled out and rectified by an increased intensity of stimulation or the use of a more lateral stimulation montage (C3/C4) where scalp edema is less prominent (Deletis, unpublished data). In general, we consider that under circumstances where the mechanism of injury to the spinal cord is purely ischemic, D wave monitoring does not add significantly to the value of muscle MEP monitoring. Gray matter is more sensitive than white matter to cord ischemia and both clinical and experimental data suggest that both peripheral and myogenic MEPs disappear earlier than the D wave when spinal cord vascularization is acutely compromised (de Haan et al., 1996, 1998; Konrad et al., 1987; Kai et al., 1994). Therefore, during thoraco-abdominal aneurysm surgery as well as during endovascular embolization of spinal cord arteriovenous malformations, muscle MEP monitoring may suffice (Sala et al., 2001; Niimi and Sala, 2002).

(6) Another relative disadvantage of D wave monitoring is the percutaneous placement of an epidural electrode when the epidural space is not surgically open, given the burden this places on the anesthesiological or surgical teams. Some authors have subdurally placed a long, small-diameter catheter a day before surgery. According to their report, they did not have serious complications such as bleeding, infections, etc. (Tamaki et al., 1986,1987).

(7) Pronounced dural adhesion during re-operation or following therapeutic irradiation of the spinal cord may prevent placement of an epidural electrode.

3.7. Monitoring of the Spinal cord dorsal columns by SEP recorded from the scalp or directly from the spinal cord

Even today, with the development of well-defined MEP methodologies, SEPs are still the most frequently used intraoperative method for monitoring the functional integrity of the dorsal column. This is a classical and well-established method and in most situations it is reliable in the operating room. Before MEPs became available for routine intraoperative use under general anesthesia, SEPs were the standard method for spinal cord monitoring. At that time it was assumed that, during surgery on diffuse lesions of the spinal cord, SEP monitoring could indirectly show that the lateral columns (CTs) were damaged.

The risk that SEPs may fail to provide information on the functional integrity of motor pathways is lower for procedures where cord integrity may be affected in its entirety. For example, during correction of spine curvature in scoliosis surgery, it could be expected that excessive stretching of neural and vascular components will affect both motor and sensory pathways. Nuwer et al., in the largest survey on SEP utility during scoliosis surgery, found that only 0.063% of patients with preserved SEPs after surgery had permanent neurological deficits (false negative results using SEP monitoring). This represents 34 patients out of 50,207 on whom the surgery has been performed. False positive results for SEPs in the same study were, 0.983% (504) patients (Nuwer et al., 1995). This is additional evidence that SEPs are valuable but they are not always sufficient to monitor all long tracts of the spinal cord. Ignoring this critical fact could have severe consequences, with a patient ending up paraplegic after surgery even when SEPs are preserved (Lesser et al., 1986; Minahan et al., 2001; Jones et al., 2003). This risk is higher for surgical procedures directly involving the spinal cord, such as ISCT surgery, because surgical maneuvers like traction, bipolar coagulation and ultrasonic aspiration can selectively injure either motor or sensory pathways.

Legatt in 2002 reviewed 7844 spinal surgical procedures, mostly in orthopedic surgery. The rate of adverse MEP changes without SEP changes was 4.1%, while adverse SEP changes without MEP changes occurred in 1.5% of the cases (Legatt, 2002). Other authors provided evidence that a combined monitoring approach using SEPs and MEPs increases the reliability of monitoring in spine surgery (Pelosi et al., 2002; MacDonald et al., 2003; DiCindio et al., 2003).

One misleading concept that has recently emerged in Intraoperative Neurophysiology, especially in spinal cord monitoring, is that SEPs should be abandoned because of their limitations and the MEPs are the only appropriate method to be used. This approach is not justified since each modality retains a great value in monitoring a specific pathway within the spinal cord. The question then centers on "What to do when MEPs are not available or unmonitorable?" Should SEPs not be used? SEPs should certainly be monitored but we have to be aware of their limitations in assessing motor pathways and the feedback from the monitoring team to the surgeon should be tailored accordingly.

3.8. Monitoring the H reflex amplitude as an indicator of suprasegmental inputs to the alpha-motoneurons

It has been shown in animals that after an acute transection of the spinal cord, or its cooling, alpha-motoneurons become hyperpolarized (Barnes et al., 1962). Based on this work, attempts have been made to indirectly monitor the motor pathways within spinal cord by recording their influence on the H reflex amplitude. It is assumed that when the motor pathways are injured, the subsequent hyperpolarization of the alpha-motoneurons will result in a significant decrease in the amplitude of the H reflex. In a group of 31 patients, Leis et al. first showed that it is possible to intraoperatively record the H reflex from the soleus muscle after stimulating the tibial nerve behind the knee, even under a regime of anesthesia that includes up to 70% nitrous oxide and up to 1.37% isoflorane (Leis et al., 1996). Following this regimen, they found that 6 of 31 patients showed a decrease in the H reflex amplitude. In 4 of 6 patients, they found moderate and transient decreases in the amplitude (up to 50% of the baseline), with no post-operative neurological deficit occurring. In 2 of 6 patients the decrease in H reflex amplitude was profound (more than 90%), and persisted throughout surgery, leading to paraplegia in both patients. The authors concluded that a profound, long-lasting decrease in the H reflex amplitude is an indicator of serious post-operative motor deficit; while moderate, transient decreases or no changes at all in the H reflex amplitude correspond with no post-operative motor deficit.

By contrast, the data collected by Slimp in a much larger group of patients ($n = 129$) showed that 5 patients (3.9%) with no changes in H reflex amplitude experienced post-operative motor deficit (false negative results) (Slimp, 2003). As in Leis's study, two patients with permanent profound changes in H reflex amplitude had motor deficits and three patients with moderate transient changes in H reflex amplitude had no neurological deficit. 93% of patients without H reflex amplitude changes showed no post-operative motor deficit.

The discrepant results in these two studies raise concerns about the validity of H reflex monitoring as a tool for predicting motor deficit.

Hyperpolarization of alpha-motoneurons, following lesioning of the suprasegmental pathways, may have a direct effect on the H reflex amplitude. Lesion(s) of suprasegmental pathways may have profound permanent effects on the amplitude of the H reflex, and such changes are not specific to CT lesions.

3.9. Anesthesia during spinal cord monitoring

The role of anesthesia during spinal cord monitoring exceeds the capacity of this review. We refer the reader to the pertinent literature (Scheufler and Zentner, 2002; Sloan and Heyer, 2002).

3.10. IOM during spinal cord procedures: a neurosurgical perspective

Within the span of neurosurgical procedures, those involving intramedullary spinal lesions are considered at high risk for post-operative deficits. Worthy of mention, in a series of 423 neurosurgical cases monitored, eventful monitoring occurred with the highest frequency in intramedullary lesions (Wiedemayer et al., 2002). The reliability of IOM during surgical procedures involving the spinal cord has significantly increased in the past few years. Before the introduction of MEP monitoring techniques under general anesthesia, only SEPs were available. SEPs have been extensively used during surgery for intramedullary spinal cord tumors. They have proven to have good sensitivity but poor specificity (Kearse et al., 1993). False negative results in intraoperative SEPs monitoring (e.g. a patient waking up with motor deficit after spinal cord tumor surgery in spite of preserved SEPs) have been recently reported in one case (Skinner et al., 2005), rare when compared with orthopedic surgery (Nuwer et al., 1995). Therefore, the chance of this event being reported in a much more uncommon procedure such as IMSCT surgery is extremely low. False negative SEPs have been reported during a number of different spinal procedures, including scoliosis surgery (Deutsch et al., 2000; Ginsburg et al., 1985; Lesser et al., 1986; Pelosi et al., 1999), anterior cervical discectomy (Jones et al., 2003), and aortic surgery (Zornow et al., 1990). On the other hand, high rates of false positive SEP changes during surgery for IMSCT (Kearse et al., 1993) imply that when MEPs are not monitored, tumor removal may be unjustifiably stopped, precluding the possibility of a complete resection.

Two more limitations of SEP monitoring are specific to IMSCT surgery. First, SEPs require averaging, which prolongs their acquisition time. During IMSCT surgery an impending injury to the cord can occur in such a short time–especially when debulking the tumor from the ventral spinal cord- that SEPs would be ineffective for providing prompt feedback to the surgeon. Second, SEPs are often lost during the initial posterior longitudinal myelotomy (Kothbauer et al., 1997; Deletis, 1999). This loss is often transient and SEP amplitude may recover before the end of the procedure when, after tumor removal, the dorsal columns are no longer laterally displaced. Even when SEPs do not recover by the end of the procedure, this event does not necessarily correlate with post-operative loss of proprioception. These observations have prompted different authors (Kothbauer et al., 1997; Brotchi, 2002) to the conclusion that preservation of SEPs should encourage a more aggressive removal, while their loss during myelotomy should never be used as a criterion for abandoning surgery. Still, preservation of SEPs correlates with better recovery due to the post-operative functional sensorimotor integration.

The inability of SEPs to provide reliable information on the functional integrity of the motor system becomes relevant if we consider that the functional integrity of motor and sensory pathways can be impaired separately. As mentioned earlier, it has been reported in spine surgery that patients may become paraplegic despite preserved SEPs (Minahan et al., 2001; Jones et al., 2003; Pelosi et al., 1999).

For all the above, there has been an emerging need for combining SEP monitoring with techniques more specifically devoted to assess the functional integrity of motor pathways. A similar approach has been suggested during supratentorial surgeries, where the corticospinal tract can be selectively damaged leaving lemniscal pathways intact, and SEP recording unaffected (Neuloh and Schramm, 2002; Szelenyi et al., 2003).

In the recent past, a few centers have started to collect intraoperative MEP monitoring data during spinal cord surgery. In 1997, using only epidural recordings of MEPs (D wave), Morota and colleagues concluded that D wave monitorability appeared as a better predictor of functional outcome than the patient's preoperative motor status (Morota et al., 1997). This observation, for the first time, introduced a neurophysiological parameter as a major predictor of outcome following IMSCT surgery. This was shortly followed by the introduction of muscle MEP monitoring providing evidence that the combination of epidural and muscle recordings of MEPs, after TES, allows for better prediction of motor outcome in spinal cord (Kothbauer et al., 1997; Kothbauer et al., 1998; Deletis, 1999) and supratentorial surgeries (Fujiki et al., 2006).

Motor evoked potentials have introduced several advantages in the IOM of spinal cord surgery. First, MEPs do not need averaging because they can be recorded and continuously updated at a rate of 1–2 Hz. This rapid feedback allows a prompt identification of impending impairment of motor pathways integrity so that the neurosurgeon can be warned in time, before irreversible injuries occur.

Second, unlike SEPs, MEPs are not compromised by the posterior longitudinal myelotomy (first surgical step to approaching a spinal cord tumor, after the dura has been opened). Third, MEPs provide specific and sensitive information on the functional integrity of the CT (D wave), while muscle MEPs supply information about the CT and the other system(s) or mechanisms involved in their generation. Relying on these techniques, false negative results (i.e. a post-operative permanent paraplegic patient despite preservation of muscle MEPs) have not occurred thus far, and false positive results (a patient being neurologically intact in spite of lost muscle MEPs) are rare (Kothbauer et al., 1997; Kothbauer et al., 1998). Fourth, in the majority of cases – with the exception of an acute anterior spinal artery syndrome – epidural and muscle MEPs deteriorate progressively, allowing corrective measures to be taken. This is a critical point since the great value of MEPs, beyond their prognostic value, relies on their ability to recognize a hazard to the motor system and therefore protect the patient from a permanent neurological deficit. Warning signals include: (a) A significant drop in muscle MEP amplitude, as compared to baseline values; a decrease in amplitude is usually more common than latency shifts. (b) A fluctuation in the response to the point that muscle MEPs can be recorded only in an on-and-off fashion. (c) A progressive drop in the D wave amplitude, approaching 50% of the initial values. Disappearance of muscle MEPs usually precedes changes in the D wave and the D wave may remain stable or drop only slightly in spite of complete muscle MEP loss.

It has been so far a consistent observation that the only point-of-no-return is when muscle MEPs are lost and D wave amplitude deteriorates below 50%. If this occurs, surgery should be immediately arrested and corrective measures should be taken to favor the recovery of MEPs. If these do not reappear, surgery should be stopped since the patient is at high risk of a complete or major long-lasting motor deficit.

Calancie et al. suggest threshold-level parameters during multi pulse TES to assess intraoperative muscle MEP changes and assist in surgical maneuvers (Calancie et al., 1998).

Muscles MEP recordings to TES are highly variable and are very sensitive to the effect of anesthesia and muscle relaxant. Thus wide variation in the amplitude and latency of muscle MEPs can be observed (Jones et al., 1996). This variability explains the lack of a linear correlation between intraoperative changes in muscle MEP amplitude and/or latency, and the motor outcome in spinal cord surgery.

More recently, other authors have suggested other criteria for muscle MEPs in order to predict post-operative outcome during IMSCT surgery (Quinones-Hinojosa et al., 2005). Alterations in muscle MEP morphology (from polyphasic to biphasic and from biphasic to loss) correlated with motor grade loss in the immediate post-operative period, at discharge and at follow-up. This study, where the D wave was not monitored, introduces muscle MEP waveform morphology as an additional criterion to assess motor pathway integrity, in addition to the all-or-none criteria proposed by others (Zentner, 1989; Jones et al., 1996; Pelosi et al., 2001; Dong et al., 2002; Kothbauer et al., 1998). Quinones-Hinojosa et al. reported that a group of 8 patients, in whom the muscle MEP changed from polyphasic to biphasic waves at the end of the procedure, presented a post-operative motor grade which was never lower than 4 out of 5 (mild impairment where joint moves against gravity and little resistance). Using these more restrictive warning criteria, the rate of total tumor removal was 57% in the entire series. The degree of removal compares unfavorably with other series (Xu et al., 1996; Constantini et al., 2000; Hanbali et al., 2002; Raco et al., 2005), especially if we consider that in the report of Quinones-Hinojosa et al. ependymomas (usually regarded as more amenable to total removal) accounted for 57% of the pathology and astrocytomas only 21% (Quinones-Hinojosa et al., 2005). It is probably justifiable to define more subtle and quantitative muscle MEP criteria that can predict post-operative outcome and prevent neurological deficits. However, from a neurosurgical and neuro-oncological stand-point, the possibility of a mild, often transient, motor impairment may be an acceptable price for the patient to pay, if this is rewarded by a complete tumor removal that, in the case of spinal cord ependymomas, cavernomas and hemangioblastomas, may mean cure of the disease. The balance between strict and loose criteria would invariably reflect the balance between false positive and false negative results. In our opinion, the use of an all-or-none muscle MEP criterion, combined with D wave monitoring, exposes the patient only to transient motor deficits and ultimately supports a more aggressive surgical attitude in the attempt to achieve complete tumor removal. When only quantitative (threshold or waveform dependent) muscle MEP criteria are used to stop surgery, there may be fewer transient motor deficits, but at the expense of incomplete removal. The need for adjuvant radiotherapy in these patients would then become an issue, in spite of the fact that radiotherapy should, nowadays, only be indicated for malignant or recurrent spinal cord tumors (Brotchi et al., 1991; Constantini et al., 2000; Jallo et al., 2003).

Recently, the anecdotal use of free running EMG as a method to detect early motor tract injury during IMSCT surgery has been reported (Skinner et al., 2005). Changes in free-running EMG anticipated TCE-MEP changes in three cases. In addition, changes in free-running EMG in two patients were the only intraoperative finding while the TCE-MEPs remained unchanged. Both patients presented a mild post-operative worsening, which completely recovered at follow-up. This report represents the first hint to the possibility of using free-running EMG criteria to improve the warning threshold and predict the value of monitoring technique during IMSCT surgery. However, the small number of patients (14 cases) does not allow any conclusion at this time about the real value of this approach. Furthermore, the fact that both of these patients with pseudo-false negative muscle MEPs identified through free-running EMG had a complete recovery at follow-up raises again the issue of how sensitive should the "ideal" MEP technique be.

Ongoing experience in the field of neurophysiological monitoring during spinal cord surgery has a valuable educational role to play which is slowly but significantly modifying some neurosurgical strategies established before the advent of IOM. We are increasingly beginning to understand the threshold of tolerance of spinal cord structures to their surgical manipulation. It is very likely that the majority of unsatisfactory results during spinal cord surgery are primarily due to ischemic derangements of the cord, secondary to its sustained traction, manipulation, rotation, and overheating produced by bipolar coagulators. Unfortunately, without the use of IOM, even the most experienced neurosurgeons will never be able to predict the degree to which the spinal cord can tolerate surgical maneuvers such as traction, bipolar coagulation and ultrasonic aspiration. Today, IOM can provide real-time neurophysiological data that can accurately assess the well-being of the spinal cord and suggest whether or not the cord is ready to sustain further manipulation. From this perspective, surgical timing is probably one of the most critical variables affecting the outcome. In other words, the same surgical maneuver (e.g. detachment of the last piece of a spinal cord ependymoma from its anterior cleavage plane proximal to perforating vessels of the anterior spinal artery) can be accomplished in an expedited non-stop fashion or may require a slower stop and go strategy. Whether one should move from one strategy to another can be suggested only by IOM data. We have repeatedly observed that if surgery is transiently stopped immediately after muscle MEPs have disappeared or the D wave has significantly deteriorated, these potentials often spontaneously recover. At this point the spinal cord is again able to endure the manipulation necessary to remove the remaining tumor. Conversely, to ignore these events and continue or, even worse, speed up the use of a Cavitron ultrasound aspirator (CUSA), or any other cord manipulation, is more likely to transform a reversible injury into an irreversible one.

Other corrective measures have proven to be of some efficacy in facilitating the recovery of MEPs during spinal cord surgery (Sala et al., 2004). There is a consistent observation, at different centers performing MEP monitoring during surgery for intramedullary spinal cord tumors, that warm irrigation of the surgical field accelerates the recovery of both SEPs and MEPs. Whether this is due to the effect of temperature, the effect of irrigation, or a combination of the two is not clear. While most of the studies reported in the literature have focused on the effect of hypothermia (Meylaerts et al., 1999, 2000; Sakamoto et al., 2003), the role played by hyperthermia on evoked potential monitoring has been less investigated (Oro and Haghighi, 1992). The possibility that irrigation per se may explain the recovery of evoked potentials is supported by experimental data on spinal cord injury models. Whenever a traumatic or ischemic injury to the spinal cord induces a disruption of the cell membranes, potassium ions accumulate in the extracellular space, counteracting the repolarization of the axons, and therefore, limiting their nerve conduction (Young and Koreh, 1986; Kwo et al., 1989; Chesler et al., 1994). Irrigation of the surgical field may – hypothetically – facilitate the washout of the extracellular potassium, and consequently, facilitate the recovery of evoked potentials.

Another mechanism of spinal cord injury during spinal cord procedures is related to ischemic derangements secondary to hypotension and or vasospasm induced by surgical manipulation. The extent to which the spinal cord can tolerate a decreased perfusion pressure is unpredictable. There is evidence, however, that even a mild drop in systolic blood pressure can affect evoked potential monitoring (May et al., 1996; Haan et al., 1997; Jacobs et al., 2000; Seyal and Mull, 2002; Sloan and Heyer, 2002; Wiedemayer et al., 2002). Under these circumstances, to pharmaceutically induce normo- to moderately hypertensive blood pressure levels, as well as the local infusion of papaverine, may result in improved spinal cord perfusion, and ultimately, facilitate the recovery of evoked potentials (Sala et al., 1999, 2004).

The corrective measures described above are easily recalled by the acronym T.I.P. (Time, Irrigation, Pressure/Papaverine) and an example of their efficacy is given in Fig. 2.

3.11. IOM during surgery for IMSCT: does it really make a difference?

> *''Advocates of most monitoring techniques point to the lack of bad outcomes as proof that their particular technique has value. Since controlled trials [...] are unlikely to occur, teleological arguments may have to be sufficient''. (Phillips and Park, Muscle and Nerve 13: 127–132, 1990)''*

This thoughtful comment by Phillips and Park can be applied to most IOM techniques used during neurosurgical procedures. It could also be stated that the real value of IOM in most neurosurgical procedures to date is not supported by Class I evidence studies (prospective randomized controlled trials), and consequently, the use of IOM techniques is still considered optional and not yet widely accepted as standard routine. A controlled trial, however, implies the designation of a ''control group'' of patients where that particular IOM technique is not used. In our opinion, very few neurosurgical centers have both the case-load of IMSCT surgery and the neurophysiological expertise to perform such a study. Even so, randomization would be arguable from both an ethical and a medico-legal perspective. Therefore, the most accurate assessment we can expect today about the real advantages of IOM techniques probably comes from historical control studies. In such studies the neurological outcome in a cohort of patients operated on with the assistance of IOM should be compared with the outcome of patients operated before the introduction of IOM techniques.

In a retrospective study on a small population of spinal cord ependymomas, operated over a 37-year period, neurological outcome in patients operated with the aid of a microscope and IOM was compared to that of patients operated before these tools were available (Asazuma et al., 1999). The authors concluded that the microscope and IOM were indispensable for improving outcome. However, the kind of monitoring used (SEPs or MEPs) is not specified and there is no data to statistically support the advantages of IOM versus those of microsurgery.

Obviously, given the major advances in Neurosurgery in terms of neuroimaging, neuronavigation, surgical devices (microscope, ultrasonic aspirator, contact laser, robotics), and neuroanesthesiology/post-operative intensive care, a comparison should be attempted, only between cohorts of patients operated on within a limited time frame. Ideally, we should only compare patients who have received exactly the same surgical treatment, except for the use of IOM. Since such a study is unlikely to occur in a prospective fashion, we have recently performed a historical-control study during surgery for IMSCTs. Both groups of patients have been evaluated based on the McCormick scale (McCormick et al., 1990). In the early post-operative period there is no difference in the neurological outcome between groups. This is due to the phenomenon of ''transient paraplegia'', which cannot be differentiated from permanent paraplegia on the basis of neurological examination alone. However, there was a significantly better neurological outcome in the monitored patients when compared to the control group, at a follow-up of about 1.5 years (range 3 to 84 months) (Sala et al., 2006).

Interestingly, there was a difference between both groups, but only in the subgroup of patients who had little preoperative neurological deficit (McCormick grade 1 to 2), while there was no significant difference in the IOM group with the more severe neurological deficits before surgery (McCormick grade 3 and 4). The reason why there were no advantages in the neurologically-impaired IOM group was that monitorability of MEPs was poor since baseline muscle MEPs were difficult to record and D waves were either absent or heavily desynchronized in the majority of cases.

These results are noteworthy. First, they provide evidence that the use of IOM may become the most relevant variable ensuring good neurological outcome for patients who undergo IMSCT surgery. Second, they suggest that, paradoxically, patients in impaired neurological conditions prior to surgery are those who can benefit less from IOM. For these patients, the preoperative neurological status still appears as the major factor affecting the outcome.

Data supporting the significant impact of IOM on spinal cord surgery has been increasingly reported by different centers around the world. However, the qualitative contribution of Intraoperative Neurophysiology is different for spinal cord than for brain surgery. In brain surgery, the value of pure monitoring techniques (SEPs and MEPs monitoring) is still scarcely recognized (Neuloh and Schramm, 2004). Undoubtedly, the major contribution recognized thus far comes from mapping techniques for the identification of functional motor, sensory and speech areas, through direct cortical stimulation. Conversely, in spinal cord surgery, monitoring techniques are by far the most relevant to the neurological outcome, while dorsal column mapping (Kržan, 2002) and CT mapping (Deletis and Camargo, 2001d; Deletis, 2006) are still experimental techniques.

Intraoperative Neurophysiology can offer different answers to different questions. Surgeons who operate on the brain basically need to localize functional tissue since brain lesions often induce plasticity or cortical reorganization phenomena. Spinal cord surgeons have the advantage that, with a few exceptions, pathways conveying important functions – such as the dorsal column and CTs – are invariably located within the cord. Unfortunately, nobody knows the extent to which these long tracts can tolerate surgical manipulation. IOM cannot replace a deep knowledge of spinal cord neurovascular anatomy, nor can it be a surrogate for a lack of technical skill. Nevertheless, IOM can provide invaluable information about the functional integrity of the cord that the neurosurgeon has to take into consideration while establishing his surgical strategy.

4. Safety issues to consider during intraoperative monitoring with MEPs

Safety concerns with intraoperative monitoring using TES have been raised (MacDonald, 2002; MacDonald and Deletis, 2007). From the extensive review of literature, unpublished clinical experience and personal communications, these papers report that out of 15,000 patients monitored using TES only a few experienced untoward effects including: one tongue–lip laceration, one mandibular fracture, five seizures, five cardiac arrhythmias, two scalp burns and one intraoperative awareness. No post-operative seizures have been reported. Most of these incidents could have been prevented with a tongue or lip protector consisting of rolled gauze. Most burns under stimulating electrodes are caused by faulty monopolar cautery leaking radiofrequency current over safety limits (Isgum and Deletis, 1998). A seizure may not always be preventable, but five seizures in 15,000 patients, when TES is used, might be an acceptable risk when compared to the incidents of seizures after direct cortical mapping using 60 Hz Penfield technique.

5. Future developments in intraoperative monitoring and mapping of the spinal cord

5.1. Dorsal column mapping (DCM) – using miniature multicontact electrode

In order to approach IMSCT, or during insertion of the tube in the spinal cord for the drainage of a syringomyelic cyst, the surgeon has to enter the spinal cord between the dorsal columns (dorsal fissure). Conventional approaches have dictated that the neurosurgeon use anatomical landmarks at the dorsal surface of the spinal cord to determine the midline. Unfortunately, the anatomical midline is very often distorted by the pathological process and is not always easily located and defined. In certain patients, pathology may displace both dorsal columns to one side (Deletis and Sala, 2001c).

The DCM method can help the surgeon find the midline between the dorsal columns on the basis of measurement of the SEP amplitude gradient recorded directly from the surgically-exposed dorsal columns. DCM is performed through a miniature multi-contact electrode consisting of 8 parallel wires, each 76 μ in diameter, separated by 1 mm, and embedded in silicon (Kržan et al. 1997,1998, 2002). This electrode is capable of recording slight differences in amplitude of SEPs between the recording surfaces after tibial nerve stimulation. The maximal SEP amplitude recorded after right and left tibial nerve stimulation is a factor that determines the functional midline of the dorsal column. Therefore, the surgeon can place the myelotomy using the Nd/YAG contact laser between the dorsal columns, preventing initial injury to them. The initial study performed on 65 patients showed promising results (Deletis and Sala, 2001c; Kržan, 2002). Controlled clinical studies are necessary to completely evaluate the potential of this method.

5.2. Mapping of the CT within the spinal cord

Monitoring the functional integrity of the spinal cord motor pathways is so far the best we can do to protect them from injury to the motor system. Further refinement of the methodology of monitoring the CT by using the D wave may still provide us with a new methodology: mapping of the CT within the spinal cord. As with all mapping methods, this one also detects the anatomical site of the CT within the spinal cord by means of the collision technique. This method depends on the fact that the D wave descending via the CT after TES can be collided and annihilated by an antidromic volley elicited by electrical stimulation of the exposed spinal cord, if the surgeon's hand-held stimulating probe comes in close proximity to the CT (TES and hand-held probe electrical stimulation of the spinal cord are performed simultaneously). D wave decrements or complete disappearance during collision indicate the anatomical location of the CT and provide a warning to the surgeon to stay away from this "hot spot". Even in the early stages of its development, this methodology has proven highly successful in identifying and localizing the CT within the spinal cord (Deletis and Camargo, 2001d; Deletis, 2006). A similar principle of collision has been used by Rothwell et al. by simultaneously performing TES and stimulating spinal cord via the epidural electrode (Rothwell et al., 1994).

6. Conclusion

Intraoperative neurophysiology of the spinal cord has become a critical part of neurosurgery and orthopedics surgery, as well as a part of clinical neurophysiology. Recent neurosurgical texts have incorporated chapters about intraoperative neurophysiology (Choux et al., 1999; Crockard et al., 2000; Black and Jaaskelainen, 2008; Pickard et al., 2004). The same is true for the books in the field of clinical neurophysiology (Daly and Pedley, 1990; Chiappa, 1997). Even specialized books that bridge intraoperative neurophysiology to neurosurgery, neurophysiology, orthopedic surgery and interventional neuroradiology have recently become available (Desmedt, 1989; Loftus and Trayenelis, 1994; Møller, 1995; Stålberg et al., 1998; Deletis and Shils, 2002a). After more than 30 years of implementation, it is intraoperative monitoring of the spinal cord that has helped to establish intraoperative neurophysiology as a clinical discipline.

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