REVIEW

State of the art : Intraoperative neuromonitoring in spinal deformity surgery

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Abstract : Application of deformity correction spinal surgery has increased substantially over the past three decades in parallel with improvements in surgical techniques. Intraoperative neuromonitoring (IOM) techniques, including somatosensory evoked potentials (SEPs), muscle evoked potentials (MEPs), and spontaneous electromyography (free-run EMG), have also improved surgical outcome by reducing the risk of iatrogenic neural injury. In this article, we review IOM techniques and their applications in spinal deformity surgery. We also summarize results of selected studies including hundreds of spinal correction surgeries. These studies indicate that multimodal IOM of both motor and sensory responses is superior to either modality alone for reducing the incidence of neural injury during surgery. J. Med. Invest. 62 : 103-108, August, 2015

Keywords **:** *intraoperative neuromonitoring, spinal deformity, IOM, neural injury*

INTRODUCTION

A decade ago, the estimated incidence of paralysis following spinal deformity surgery was 0.25% to 3.2% (1-3). Intraoperative neuromonitoring (IOM) is now widely accepted to reduce the risk of neurologic complications in spinal surgery and thoraco-abdominal aortic aneurism surgery. Various IOM modalities allow continuous functional assessment of the neuromuscular junction, peripheral nerves, spinal cord, brainstem, and cortex during spinal surgery. Although IOM generally refers to neurophysiological monitoring, the Stagnara wake-up test, which provides direct evaluation of the patient's motor functions without specialized equipment, is still used when necessary. Among the various IOM techniques available, somatosensory evoked potentials (SEPs), muscle evoked potentials (MEPs), and spontaneous electromyography (free-run EMG) are most frequently used in clinical practice.

Deformity correction surgery is effective for such spinal disorders as scoliosis (idiopathic, congenital, neuromuscular, and syndrome-related), exaggerated kyphosis, and lordosis, but iatrogenic spinal cord injury is still a feared complication. The estimated incidence of neurological complications for such surgery is 1% according to the Scoliosis Research Society, and increases to 1.87% when a combined surgical approach is used (4). The main causes of iatrogenic neurologic sequelae are implant-related damage, such as breach of a pedicle screw into the spinal canal or foramen, and injury during correction maneuvers, including distraction, compressive force to correct deformity, and the rod rotation technique to translate the vertebra.

This review summarizes the clinical applications of IOM techniques and describes the efficacy of each for detecting and reducing iatrogenic injury during spinal deformity surgery.

SOMATOSENSORY EVOKED POTENTIALS

SEPs, first recorded by George Dawson in 1951 (5) but not used clinically until 1977 (6), are evoked by distal surface electrodes placed on the upper or lower limbs and recorded at the scalp, spinal cord, and/or sites proximal to the stimulation electrode. SEPs are classified into 3 types according to latency : short-latency SEPs (SSEPs), middle-latency SEPs, and long-latency SEPs (7, 8). Among these, SSEPs are utilized most frequently to monitor the functional integrity of afferent sensory nerve inputs to the spinal cord and transmission to the cortex. SSEPs reflect action potential transmission from the periphery through Aβ fibers that carry non-nociceptive sensory information. The most common sites for stimulation are the median and ulnar nerves for the upper extremities and the posterior tibial nerve for the lower extremities (3, 9, 10). Sensory impulses from the upper extremities are conducted to the spinal cord through peripheral nerves and the brachial plexus, where the Erb's point potential is generated (11). Sensory impulses from the lower extremities travel past the popliteal fossa, where the potential is generated, before reaching the lumbosacral plexus and entering the cauda equina, where a lumbar potential is generated. In all cases, impulses continue along the dorsal root and enter the posterior spinal cord (11). SEP recording is widely applied clinically for IOM because numerous potentials can be reliably evoked and recorded using noninvasive surface electrodes (12).

Scalp recording electrodes are often placed at CP3 and CP4 (intermediate between C3 and C4 and between P3 and P4, respectively) according to the international 10-20 scalp positioning system (Figure 1). The level of spinal surgery determines the choice of stimulation and recording sites. In cervical spine surgery, median nerve SSEPs are monitored, while in thoracic or lumbar surgery, tibial SSEPs are monitored. An additional recording site over the popliteal or supraclavicular space provides a control signal that allows the monitoring team to determine whether the recording system is functioning properly.

There are many factors affecting the amplitude and latency of SSEP waveforms (13). Physiologic factors that may influence evoked potentials (EPs) include body temperature, blood pressure, hematocrit, acid-base balance, and oxygen and carbon dioxide tensions

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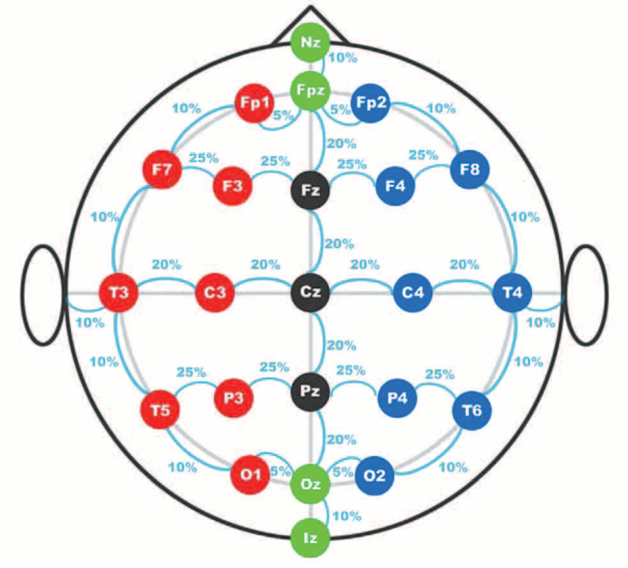


Figure 1.
The international 10-20 scalp positioning system showing the locations of scalp electrodes for measuring the evoked potentials.

(14). Hypothermia may increase false negatives (13). Most anesthetic agents depress evoked response amplitude and increase latency, which makes intraoperative neurophysiologic monitoring more difficult. All halogenated inhalational gases produce a dose-dependent increase in latency and reduction in amplitude of cortically recorded SSEPs (15, 16). The anesthetic gas nitrous oxide reduces SSEP cortical amplitude both when used alone and when combined with halogenated inhalational agents, opioids, or propofol (17-19).

The first application of SSEP recording for spinal deformity surgery was described by York *et al.* in 1987 (20). They reported transient intraoperative loss of SSEP during distraction, spine manipulation, anesthesia, and hypotension, but all patients that had an SSEP within ±2 standard deviations of anesthetized control values by the end of surgery had no lasting neurologic complications. While an amplitude decrease of 50% resulted in no neurologic sequelae, over a 50% decrease would indicate dysfunctional sensory pathways and potentially complete spinal cord compromise. A survey by the Scoliosis Research Society and the European Spinal Deformities Society documented a reduction in injury rate ranging between 0.7% and 4.0% prior to the introduction of SSEP monitoring to less than 0.55% with SSEP monitoring (2). Nonetheless, false-negative cases with spinal cord injury still occur despite such monitoring (2, 21). For example, the primary SSEP conduction pathway is the dorsal column, so tibial nerve SEPs can remain unchanged even when there is damage to the anterior spinal cord, such as that caused by ischemia in the territory of the anterior spinal artery (ASA) (21). Such cases underscore the importance of motor response IOM. Thus, a major potential weakness of SSEP monitoring is low sensitivity to evolving motor deficits due to direct corticospinal tract damage or ASA damage/occlusion (22).

MOTOR EVOKED POTENTIALS

Although intraoperative SEP monitoring has been used for over 25 years to identify neurological deficits and has proven effective in reducing iatrogenic spinal cord injury, there have been a number of reports of false negatives with SEPs (23-25). MEP recording techniques were devised to circumvent the limitations of SEP monitoring. MEPs are the electromyographic responses of peripheral muscles to electrical stimulation of the motor cortex. Patton and Amassian laid the scientific foundation for MEP monitoring in 1954 by discovering that a single electric pulse applied to monkey motor cortex evoked several descending corticospinal tract volleys (26). Direct monitoring of the corticospinal pathway in conscious humans became possible with the work of Merton and Morton in 1980 (27).

A major advantage of MEP monitoring during spinal surgery is that it allows for detection of ischemia in the ASA territory. The spinal cord is supplied by the ASA and the posterior spinal artery (PSA), with motor tracts primarily supplied by the ASA and sensory tracts primarily by the PSA. Thus, as mentioned, SEPs can be preserved in the event of ASA damage or occlusion because the primary conduction pathway is the dorsal column. Moreover, the use of MEP monitoring, particularly in spinal surgery, is more strongly correlated with good postoperative motor outcome than SEP monitoring, so many experts advocate MEP monitoring for all spinal surgeries (28).

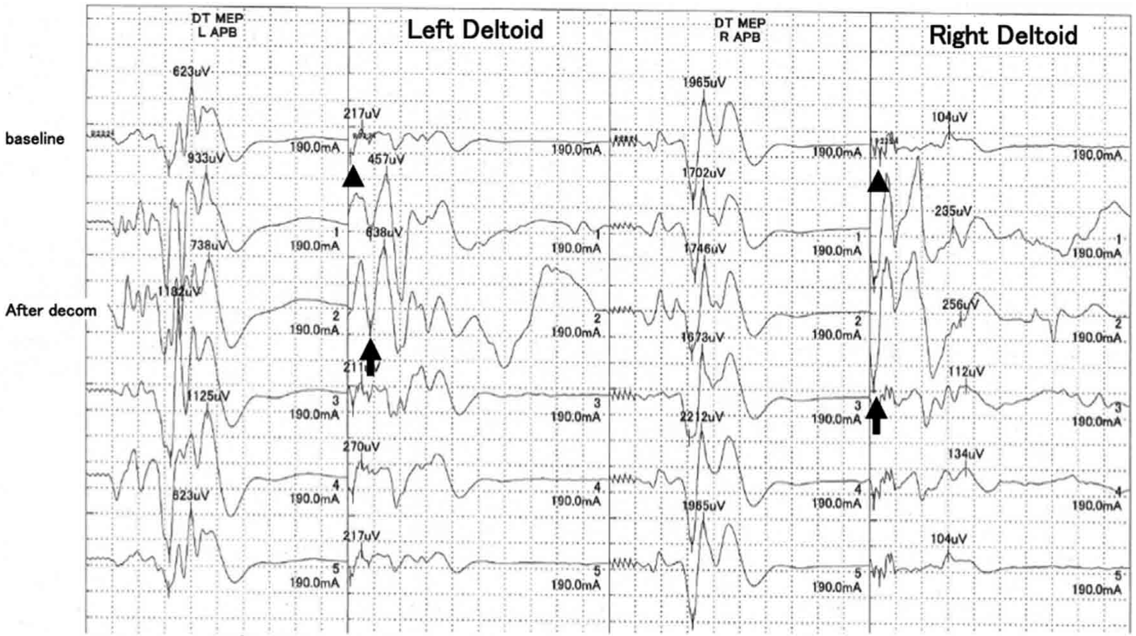
A single electrical stimulus applied to the motor cortex results in descending volleys in the cortico-spinal tract and evokes large amplitude muscle responses recordable by subdermal needle electrodes placed in distal limb muscles, provided that the motor neuron pool is sufficiently excitable. Previously, a single stimulating MEP was used (27, 29, 30). Under general anesthesia, however, a single stimulus may not be effective since I-waves, which represent the volleys produced by the cortical neurons, are diminished. Indeed, this method has produced many false results. In response, constant-current multipulse stimulation was developed in which 4 to 6 stimuli are delivered at interstimulus intervals of 2.0 ms (31).

A number of additional MEP recording techniques have been devised, including direct stimulation of the rostal spinal cord and transcranial magnetic or electrical stimulation, the latter being particularly suitable due to relatively low invasiveness. In fact, transcranial electrical stimulation (TceMEP) is now the most common MEP modality for intraoperative monitoring of descending motor pathways. The stimulating electrodes for TceMEPs are placed 2 cm anterior to C3 (C3'), C4 (C4'), Cz (Cz'), C1, C2, and Fz according to the international 10-20 scalp positioning system (Figure 1). The descending motor pathways run primarily in the lateral columns of the spinal cord. The standard montage is C3/C4 for eliciting MEPs in the upper extremities and C1/2 for eliciting MEPs in the lower extremities (32).

One weakness of MEP monitoring is that neuromuscular blockade must be minimized or avoided. Furthermore, among EPs, the MEP is most sensitive to anesthetic agents. For this reason, the use of halogenated anesthetics and nitrous oxide should be avoided ; rather, total intravenous anesthesia with propofol is preferred over inhalational agents when monitoring muscle MEPs (33, 34). Pahys *et al.* reported that mean arterial blood pressure less than 50 mmHg can also influence MEPs (35), and recommended maintaining mean arterial blood pressure above 80 mmHg to eliminate false results. Other disadvantages include the risk of tissue injury to the patient and inadvertent shock to operating room staff as the simulating electrodes are at high voltage and carry large currents. MEP monitoring also carries the risk of tongue bite due to direct stimulation of the trigeminal nerve. There is also a small risk of seizures, and the monitorist should be vigilant and the surgeons aware of this possibility (11).

We introduce some cases of IOM using TceMEPs.

Case 1. A patient with ossification of the posterior longitudinal ligament of the cervical spine underwent posterior laminectomy and fusion from C4 to C6 due to myelopathy. After decompression, the latency of the left deltoid was delayed more than 10% relative to baseline, while the latency of the right deltoid remained within the normal range (Figure 2). However, the amplitude of the left



No.	Time	L APB N1 Lat[ms]	N1-N2 Amp,Dif[%]	N2 Lat[ms]	Left Deltoid N1 Lat[ms]	N1-N2 Amp,Dif[%]	N2 Lat[ms]
BL	baseline	60.1	623.5	51.5			
BL	baseline				25.4	217.2	20.9
BL							
BL							
1		65.7	150	56.6	34.6	210	28.7
2	After decom	66.8	118	50.0	33.9	294	28.7
3		55.3	190	52.3	25.5	97	22.1
4		66.4	181	51.9	25.4	124	22.0
5		60.1	100	51.5	25.4	100	20.9

No.	Time	R APB N1 Lat[ms]	N1-N2 Amp,Dif[%]	N2 Lat[ms]	Right Deltoid N1 Lat[ms]	N1-N2 Amp,Dif[%]	N2 Lat[ms]
BL							
BL							
BL	baseline	56.0	1965.0	52.0			
BL	baseline				50.3	104.3	23.8
1		55.9	87	52.8	52.0	226	21.6
2	After decom	56.4	89	51.7	54.9	246	21.6
3		55.6	85	50.8	57.0	107	21.7
4		55.5	113	51.8	56.9	129	21.7
5		56.0	100	52.0	50.3	100	23.8

APB: abductor pollicis brevis; decom: decompression; Lat: latency; Amp: amplitude

Figure 2.
Intraoperative MEP waveforms of Case 1 showing an increase in latency measured at the left deltoid from 25.4 ms (arrowhead) at baseline to 33.9 ms (arrow). The right deltoid showed no significant change in latency.

deltoid did not reduce. The patient awoke with pain in the left upper arm and left deltoid weakness (manual muscle test score of 1), so-called "C5 palsy". Myelopathy improved and C5 palsy resolved by 6 months after surgery.

Case 2. A 67 year-old male patient with non-dysraphic intradural lipoma in thoracic spine underwent laminectomy and resection of tumor. After resection of approximately 20-30% of the tumor, a loss of> 60% of the amplitude of the TceMEP of left TA was observed (Figure 3). We stopped the resection, and duraplasty with an autologous fascia was conducted. Recovery and improvement of MEP were confirmed postoperatively (36).

SPONTANEOUS (FREE-RUN) EMG MONITORING

Free-run (continuous) EMG activity from a muscle is recorded when peripheral nerves or roots are at risk of injury during spinal surgery (37). When nerves are stretched or compressed, axons are depolarized, resulting in spontaneous action potentials that produce contraction of muscle fibers. By measuring these contractions using electrodes placed in the muscle, surgeons can modify the operative procedure in a timely manner to avoid nerve root injury. The main weaknesses of free-run EMG are the high rate of false positives, high sensitivity to body temperature changes, and contraindication for neuromuscular blockade.

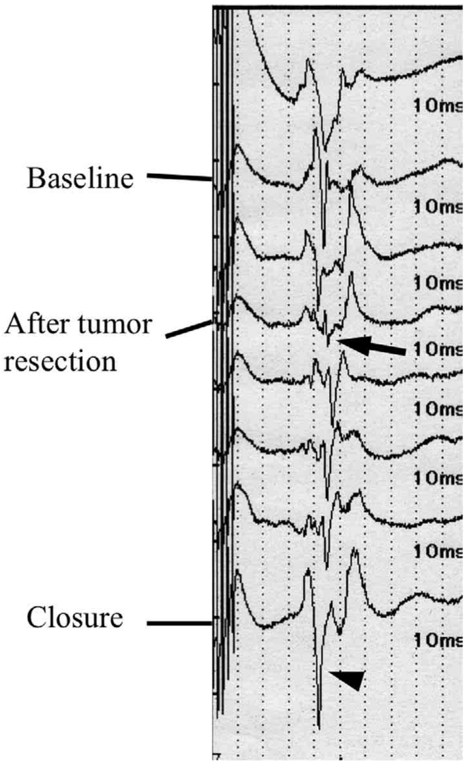


Figure 3.
Intraoperative MEP waveform of Case 2 showing a loss of> 60% of the amplitude of the TceMEP of left TA (arrow), and recovery of MEP at closure (arrowhead).

INTRAOPERATIVE NEUROMONITORING IN SPINAL DEFORMITY SURGERY

The development of IOM has minimized postsurgical neurological complications by reducing the incidence of inadvertent spinal cord injury (1, 3, 20, 24, 38-49). However, spinal deformity correction procedures, including pedicle screw insertion, vertebral distraction, rotation, osteotomy, and kyphosis correction still carry significant risks of spinal cord injury due to direct neural injury or vasculature damage, resulting in sequelae ranging from minor sensory disturbance to permanent paraplegia. Several studies including many hundreds of spinal deformity correction surgery cases are summarized in Table 1 for neurological deficit, true positive, true negative, false positive, and false negative rates (Table 1) (24, 40, 41, 47, 49-51). The definition of true positive varied across these studies. Here, we defined true positive as follows : (1) significant signal changes accompanied by a new postoperative neurologic deficit, (2) significant signal deterioration resulting from a recognized surgical maneuver, or (3) signal improvement to baseline after a specific intraoperative intervention. Cases due to hypotensive episodes or poor electrode positioning were not considered true positives. In contrast, the definitions of true negative, false positive, and false negative were reasonably consistent across these studies. Using the criteria above, we re-calculated the true-positive rate for each study and found that postoperative neurological deficits occurred in 0.4% to 2.7% of patients. False-negative results, in which IOM showed no change from baseline but the patient demonstrated an immediate postoperative neurological deficit, were reported in two of these studies, one using multimodal monitoring of SEP and MEP (46) and the other using SEP alone (47, 50). The overarching goal of MOI is to avoid false-negative results since this provides the surgeon no opportunity to alter operative procedures and avoid serious neurologic deficit. In these studies, multimodal monitoring (MIOM) showed better results than single modality (SEP or MEP) monitoring for prevention of postoperative neurological deficit (0.4%-0.6% for MIOM vs. 0.6%-2.7% for single IOM). In these MIOM cases, SEP signal changes lagged behind changes in MEP by an average of 5 min (24). Thus, MEP provided an earlier alert to the surgeon and may have facilitated more rapid correction to mitigate an evolving injury. However, these studies used no standardized warning criteria for MEP and SEP and there was no consistency in interpretation of the results. Moreover, all used a variety of intervention methods. For instance, some studies conducted the wake-up test in cases of changing MEP and/or SEP

Table 1 : Result of studies of IOM in spinal deformity surgeries.

Reference	Diagnosis	No. of cases	Method	Alarm point		Neurologic deficit rate	Alarm rate	True Positive	True Negative	False Positive	False Negative
				SEP	MEP						
Zhuang 2014	spinal deformity	1162	MEP	-	amp : > 80% down	1.3%	4.4%	1.3%	98.4%	0.26%	0.0%
Thirumala 2014	idiopathic scoliosis	477	SEP	amp : > 50% down or latency : > 10% up	-	0.6%	4.2%	2.1%	95.8%	1.9%	0.2%
Thuet 2010	pediatric spinal deformity	3436	SEP, DNEP	amp : > 60% down or latency : > 10% up	amp : > 80% down or latency : > 10% up	0.6%	-	2.2%	-	-	0.2%
Kundnani 2010	adolescent idiopathic scoliosis	354	SEP, MEP	amp :> 50% down or latency : > 10% up	amp : > 65% down or latency : > 10% up	0.56%	3.7%	3.1%	96.3%	0.6%	0.0%
Schwartz 2007	adolescent idiopathic scoliosis	1121	SEP, MEP	amp : > 50% down	amp : > 65% down	0.8%	3.4%	2.6%	96.6%	0.8%	0.0%
Padberg 1998	idiopathic scoliosis	500	SEP, NMEP	amp : > 60% down or latency : > 10% up	amp : > 80% down or latency : > 10% up	0.4%	1.8%	0.4%	98.2%	1.4%	0.0%
Forbes 1991	spinal deformity	1168	SEP	amp : > 50% down	-	2.7%	7.2%	2.7%	92.8%	4.5%	0.0%

IOM : intraoperative monitoring, amp : amplitudeAlarm signals (41, 47, 49, 50), while others did not (24, 40, 51).

Although MEP monitoring is widely considered the gold standard for monitoring the functional integrity of motor pathways (28), a few case reports have reported false negatives, resulting in neurological deficit. Modi *et al.* reported such a case of false-negative MEP monitoring during scoliosis surgery, resulting in a permanent postoperative neurological deficit (52). They speculated that massive blood loss (> 9000 mL) was the probable cause of ischemic spinal cord injury. Hong *et al.* reported cases of false-negative and delayed false-positive MEP signals in a series of operations. Fortunately, there was no further neurological deficit at final follow up. In both studies, MEP alone was used to monitor intraoperative spinal cord function, and both concluded by recommending combined MEP and SEP monitoring to reduce the incidence of false-negative cases.

CONCLUSION

Considering the above, we now apply IOM to complicated spine surgeries, such as decompression and fusion for OPLL in cervical and thoracic spine, scoliosis correction surgery, spinal tumor resection surgery, which have potential risks of intraoperative and postoperative neurological complications.

The available evidence suggests that MIOM is more effective and reliable than single modality MOI for detection of intraoperative spinal cord injury during spinal correction surgery. However, no MOIM regimen is perfect, and ethical issues have limited randomized control trials evaluating IOM efficacy. Surgeons, anesthesiologists, and other operating room professionals should be knowledgeable on the applications, mechanisms, advantages, and limitations of different IOM techniques.

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