Surgeon directed transcranial motor evoked potential spinal cord monitoring in spinal deformity surgery:

A review of viability, safety and efficacy

Dr. Ramanare Magampa (MMed dissertation)

Student number: MGMRAM001

University of Cape Town

Master of Medicine MMed: Orthopaedics

Department of Orthopaedic Surgery: University of Cape Town/ Groote Schuur Hospital, Cape Town, South Africa

Email: magampa@gamil.com

Telephone number: 0845152233

Table of contents **page**

Declaration

DECLARATION

I, [illegible], hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature: Signed by candidate

Date: 9/6/20

Acknowledgements

Supervisor and co-author:

Prof. Robert Dunn

Head of Department of Orthopaedic Surgery: University of Cape Town/ Groote Schuur Hospital, Cape Town South Africa

Email: robert.dunn@uct.ac.za

Format

Publication format

Intended journal

The Bone and Joint Journal

<u>Chapter 1</u>

<u>Literature Review</u>

Introduction

Spinal deformity surgery carries a reported risk of neurological injury between 1.5% to 9%, climbing with complexity and congenital aetiology of the deformity [1, 2]. This neurological loss of function may be transient or permanent, the latter resulting in a devastating impact on the patient, their family and the surgeon.

The scoliosis research society conducted a survey investigating the acute neurological complications in the treatment of scoliosis in 1975. It was published in the journal of bone and joint surgery by MacEwen GD, Bunnell WP and Sriram K where they found the incidence these complications to be 0.72 %.[1] However, the 1975 the indications, thresholds and goals for surgery differed from current parameters as did the instrumentation and techniques available to do so.

Weis and Goodall performed a systematic review of PubMed literature in 2008 where they investigated the rate of complications in scoliosis surgery. Looking specifically at the incidence of neurological complications occurring in different scoliosis aetiologies they found that idiopathic scoliosis had the least with 1.5%, mixed aetiology 2.7%, adult scoliosis 7.5% and congenital scoliosis 9%. [2]

The most basic and definitive assessment of neurological function is performed by doing the wake-up test, which was first published by Vauzelle, Stagnara and Jouvinroux in 1973. It involves fully waking the patient up during the surgery and asking them to voluntarily move first the upper limbs and then the lower limbs. The disadvantages of the test are unintended extubation, loss of IV access and patient recall. Hoppenfeld et al published on the ankle clonus test for assessment of the integrity of the spinal cord during operations for scoliosis in the JBJS in 1997. Ankle clonus was described by Dimitrejevic et al. as a "hyper-reflexic state often associated with spasticity and upper motor neuron lesions. This was found to be present bilaterally in patients recovering from general anaesthesia. Reversal of anaesthesia occurs in stages with the return of lower motor neuron function occurring first and causing an imbalance that is clinically detectable via the ankle clonus test. The presence of ankle clonus is indicative of intact spinal cord function and can be performed before the patient is able to move or respond to verbal stimuli. This study showed the test to have sensitivity of 100% and a specificity of 99.7%. [3]

Neurophysiological monitoring was first introduced in the 1970 with somatosensory evoked potential (SSEP) monitoring, which monitor the electrophysiological responses of the nervous system to sensory stimuli. Stimulation of distal peripheral nerves results in a chain of electrical events which are transmitted up the spinal cord to the frontoparietal somatosensory area of the brain. The American Electroencephalographic society published guidelines in 1984 describing the precise technique to perform SSEP monitoring as it is a complex process with a spectrum of protocols involving different stimulation and recording sites which aim to limit errors. An example of such demonstrated by Owen et al is the rate of false positives dropped from 28% to 9% when an additional cervical recording site was added to a standard SSEP setup. There are publications and case reports, Lesser et al Annuls of Neurology 1986, and Ben-David et al Spine journal 1987, documenting false negatives, where patients with normal traces awoke with neurological fallout. In the 1980s the incidence of false negatives was as high as 5% but as the knowledge and understanding of SEP monitoring grew so the rate of false negatives decreased as documented in the 1995 multicentre study by Nuwer with a reported incidence of 0.13%. Ginsberg et al in1985, Bridwell et al in 1998 and Schwartz et al in 2007 all showed that sole SEP monitoring had a very low sensitivity ranging from 25% to 43%. [4,5,6,7]

Motor evoked potentials (MEP), first described in the 1980s by Merton and Morton, are produced by a synchronised excitatory volley in the corticospinal tracts which is activated by either magnetically or electrically derived stimuli applied to the brains motor cortex via the scalp, transcranial motor evoked potentials(TcMEP), or directly on the spinal cord via the spinous process or in the epidural space.[8] This stimulation travels down the central nervous system to the peripheral nervous system and terminates in the motor unit resulting in a muscle response. Myogenic motor evoked potential monitoring utilises electrodes placed on or in desired peripheral muscles whilst neurogenic motor evoked potentials monitors responses obtained from peripheral nerves using subdermal needles. Although sensory loss is a negative complication, motor loss results in more devastating sequelae. SEP traces indirectly asses motor function as their preservation has been shown to correlate with normal motor function whilst MEP directly assess the motor pathways [7-10,12-17]

Luck et al evaluated and published in the Spine journal in 2001 various evoked potential techniques in scoliosis surgery. They found that motor-evoked potential monitoring as demonstrated by cortical motor-evoked potential and spinal cord evoked potentials had no false negatives or false positives whereas all SSEP type monitoring displayed both false negatives and positives [9]

Hsu et all in the Spine journal in 2008 showed transcranial motor evoked potential monitoring, used as a sole monitoring modality in spinal deformity surgery, had a sensitivity of 1.0 (95% CI: 0.66–1.0), specificity 0.97 (95% CI: 0.93–0.99), negative predictive value of 1.0 (95% CI: 0.96–1.0), and positive predictive value of 0.67 (95% CI: 0.39–0.87).[10]

The scoliosis research society issued a policy statement in 1992 advocating the use of neurophysiological monitoring to assist in early detection of complications and possibly prevent post-operative morbidity in patients undergoing spinal surgery. Neurophysiological monitoring is considered as a viable alternative and adjunct to the use of the wake-up test and ankle clonus test [11]

SSEP and MEP monitoring are the fundamental methods of neuromonitoring, and their use has evolved and specialised to allow for better investigation and interpretation of spinal cord function. Apart from improvements in understanding and techniques, this evolution resulted from utilization of different stimulus zones and response assessment sites and by using them in combination or synchronously. This multimodal intraoperative neuromonitoring (MIONM) approach has been shown, by Pelosi et all in 2002, to be superior to single monomodal techniques in increasing the ability to monitor the spinal cord even in patients with pre-operative dysfunction and for improving its sensitivity and predictivity. In this study they found that no patient with unchanged or transient MEPs that recovered had new motor deficits.[13]. Ito et al in 2016 performed a multicentre study assessing MIONM that showed that any combination that included MEP has sensitivities of more than 80%.[12] However the lower sensitivity is attributed to the fact that this study incorporated all spinal surgery including orthopaedic and neurosurgical procedures with the latter carrying far more risk and expected spinal cord injury.

Rationale for study

Although ideal neuromonitoring involves multimodal intraoperative neuromonitoring, the logistics of its setup and interpretation require a neurophysiologist to be present at all times and an in depth understanding of this process by the anaesthetic team.[17] Apart from being labour intensive and time consuming having a neurophysiologist adds significant costs to the procedure and this difficulty is further compounded by the fact there are very few qualified and available in South Africa. In our current resource constrained environment, it is difficult to justify this additional cost especially when most cases have normal electrophysiological status throughout.

Sole transcranial motor evoked potential monitoring has gained popularity in recent years with an increase in publications proving its safety, efficacy and its ability to reassure the surgeon to confidently perform spinal deformity surgery. These publications however all seem to use neurophysiologists or other technically trained and competent staff to assist in the setup and interpretation of the transcranial motor evoked potentials monitoring.

Our Groote Schuur Hospital / University of Cape Town spinal deformity surgeon is utilizing a system that is entirely setup, directed and interpreted by the surgeon. The surgeon is thus wholly responsible for this process with only intermittent directions and instructions given to operating room personnel to initiate stimulus runs by pressing the enable and start buttons on the laptop. There is only one article in the available literature specifying surgeon directed transcranial monitoring and it is the 2016 Pickell et al study published in the Journal of Spine Surgery. They use a very similar protocol with the surgeon setting up and in interpreting the TcMEP monitoring. This study found that changes in TcMEP traces alerted the surgeons to possible cord injury thus allowing them to make adjustments, revisions and reversals that resulted in no patients having post-operative fallout.

They concluded that “surgeon-driven neuro-monitoring was a safe and effective means of intraoperative neuro-monitoring during spinal surgery. It reliably detected intraoperative insults, which could potentially have resulted in postoperative neurologic compromise, and was not associated with any false-negative results in this cohort. Utility of surgeon-driven monitoring, using validated algorithms, may provide an option for this added safety measure even in cases where monitoring personnel are unavailable.” [14]

The aim of our review was to present our experience using surgeon directed TcMEPs, assessing its viability, safety and efficacy.

Methods and Intra-operative monitoring

The NIM-SPINE System developed by Medtronic is a powerful, multi-modality neural integrity monitor that includes both the technical capabilities demanded by monitoring professionals and the ease of use features necessary to allow the surgeon to directly monitor the patient’s nerve root and spinal cord function. The system provides two types of monitoring modalities, electromyographic (EMG) and motor evoked potential (MEP), and intuitive audible and visual real-time feedback to aid in intraoperative decision-making.

Analysis of the surgeon’s setup and technique confirmed that they were in keeping with published and widely accepted protocols for cortical electrically derived motor evoked potential monitoring. The Nim-Eclipse Spinal

System (Medtronic) was used in all cases. Once the patient was asleep, transcranial corkscrew electrodes were placed on the vertex over the cortical motor strip in line with the ears a few centimetres either side of the midline. Needles were placed bilaterally in the thenar muscle bulk and medial to the 5th metacarpal, as well as in the feet medially inferior to the 1st metacarpal (abductor halluces) and subcutaneously on the dorsum. [4,7,8,9,11-16]

The protocols in TcMEP interpretation involve initially establishing a baseline trace to allow for accurate referencing of trace abnormalities[4,,7,8,9,11-16] Calanice et al in the Journal of neurosurgery in 1998, published an article confirming that threshold level multi-pulse transcranial stimulation of the motor cortex was a safe, sensitive and specific way of monitoring motor conduction of motor pathways. This technique provided immediate feedback and significantly decreased the need for high stimulus intensities that were traditionally used to elicit muscle contractions and confirm intact motor pathways, as they had the negative effects of patient movement and electrical burns. [14]

The anaesthetist oversees the patient's physiological status, and this plays an integral part in part in the function of the nervous system meaning anaesthetic understanding of the process is vital for successful neuromonitoring. Apart from its usual responsibilities, anaesthesia in neuromonitoring cases has be designed to maximize signal acquisition. Physiological parameters like body temperature, blood pressure, hypovolaemia, oxygenation and haemoglobin level all affect signal negatively and their optimization is paramount for a reliable trace. Somatosensory evoked potential monitoring is less sensitive to general anaesthesia, but this benefit is limited by the superior sensitivity and specificity of motor evoked potentials as already discussed in this review. Mostly all anaesthetic agents (inhalational halogenated gases and nitrous oxide) decrease signal amplitude and increase signal latency thus impairing the obtained signal and negating the reliability of monitoring. Exceptions are the intravenous agents etomidate, ketamine and propofol which at the correct dosages have minimal effect on signal trace, although some studies have shown dose dependant negative changes at higher dosages. Opioids have also been shown to have minimal impact on signals in lab studies with notably the newer synthetics showing no effect on traces at the correct doses. Opioids however are suppressive and may diminish the patient's overall physiology and thus limit the patients waking up and thus the clinical examination. [17-20]

Vitale et al published in the 2010 Journal of Bone and Joint Surgery a study investigating the risk factors for spinal cord injury during spinal deformity surgery. In this study they found that true electrophysical events corresponded both anatomically and temporally with either the surgeon's or anaesthetist's intraoperative action. The primary anaesthetic intraoperative factor was hypotension whilst surgeons' factors included deformity correction, malposition of pedicles screw and direct spinal cord trauma. There was no case with a true electrophysical event that could not be attributed to an intraoperative action.[18]

Pre-existing neurological fallout is always a concern as obtaining reliable trace can be difficult at times. Patients with complete spinal cord discontinuity obviously have no recordable trace below the level. The difficulty comes when there is a pre-existing neuromuscular condition or partial dysfunction. Dicindio et al published in the Spine journal in 2003 a study on spinal cord monitoring in patients with cerebral palsy associated scoliosis and other neuromuscular scoliosis. This study looked at both somatosensory and motor evoked potential monitoring and found 100% of patients with mild and moderate cerebral palsy had obtainable baseline traces with both modalities

.In severe cerebral palsy traces were obtained in 70% of cases with SSEP and 90% of cases with TcMEP whilst in other neuromuscular scoliosis cases baseline traces were obtained in 86% of cases via both modalities. [22]

The major safety concern when using transcranial motor evoked potential monitoring is the induction or worsening of seizures in patients with pre-existing epilepsy and other seizure conditions. Salem et al published a study in the European spine journal in 2016 where they found that TcMEP did not induce intra operative or post-operative seizures nor did it contribute to deterioration of seizure control.[21]

The most difficult and complex spinal deformity surgery is a vertebral column resection. Iyer et al performed a systematic review of complications and outcomes following adult vertebral column resection. Eleven studies met the inclusion criteria, with neurological complication being the most reported complication. They found the incidence of all neurological injury in the selected articles to be 13.3% with a range of 6.3%-15.8%.[23]. Severe angular kyphosis increases the complexity of vertebral column resection surgery as demonstrated by the high incidence of neurological injury of 35% as published by Atici et al in the Acta Orthopaedica et Traumatologica Turcica journal in 2017[24]

It is well known from multiple studies that spinal cord injury occurs via 4 mechanisms that include mechanical compression, cord distraction, pure vascular insult or a combination of all. The Bridwell study published in the Spine journal in 1998 found that the final common pathway was vascular as cord compression and distraction all lead to ischaemia.[25].A study looking at the direct link of the effects of abnormal TcMEP traces and spinal cord function in humans would be completely unethical as this would surely result in patient paralysis. It is for this reason that the only studies examining this were performed on animal models. Morris et al, published in the Spine journal in 2015, using rat models showed that if the spinal cord compression was removed immediately, normal post-operative function was detected, but if compression lasted more than 5minutes after complete loss of signal amplitude significant deterioration in functional testing was observed when compared with preoperative baseline values.[26]

Study aims

The aim of this article is to present our experience using surgeon directed TcMEPs, assessing its viability, safety and efficacy. Although TcMEP monitoring is a well described, published and practised modality, there is only one article in the published literature looking at surgeon driven/directed transcranial motor evoked potential monitoring. Resource constraints, economic factors and paucity of literature mean further research and evidence are required to propel this novel surgeon operated technique to acceptable standard practice.

References

(1) MacEwen GD, Bunnell WP,Sriram K,. Acute neurological complications in the treatment of scoliosis. A report of the Scoliosis Research Society. The Journal of bone and joint surgery. American volume 1975;57(3):404-8.

(2) Weiss HR GD,. Rate of complications in scoliosis surgery - a systematic review of the Pub Med literature. Scoliosis 2008;3.

(3) Hoppenfeld S, Gross A, Andrews C, Lonner B. The ankle clonus test for assessment of the integrity of the spinal cord during operations for scoliosis. The Journal of bone and joint surgery. American volume 1997;79(2):208-12.

(4) Padberg AM, Wilson-Holden T, Lenke LG, Bridwell KH. Somatosensory and Motor Evoked Potential Monitoring Without a WakeUp Test During Idiopathic Scoliosis Surgery: An Accepted Standard of Care. Spine 1998;23(12).

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

(6) Lesser RP, Raudzens P, Lüders H, et al. Postoperative neurological deficits may occur despite unchanged intraoperative somatosensory evoked potentials. *Ann Neurol*1986;19:22–5

(7) Macrì S, De Monte A, Greggi T, Parisini P, Zanoni A, Merlini L. Intra-operative spinal cord monitoring in orthopaedics. Spinal Cord 2000 03;38(3):133.

(8) Merton PA, B Morton ,H. Stimulation of the Cerebral Cortex in the Intact Human Subject. ; 1980.

(9) Luk KD, Hu Y, Wong YW, et al. Evaluation of various evoked potential techniques for spinal cord monitoring during scoliosis surgery. *Spine* 2001;26:1772–7

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

(11) Scoliosis Research Society position statement. Somatosensory evoked potential monitoring of neurologic spinal cord function during spinal surgery. Scoliosis Research Society, Kansas City, Missouri, September 1992.

(12) Ito, Zenya, Matsuyama, Yukihiro, Ando, Muneharu, Kawabata, Shigenori, Kanchiku, Tsukasa, Kida, Kazunobu, Fujiwara, Yasushi, Yamada, Kei, Yamamoto, Naoya, Kobayashi, Sho, Saito, Takanori, Wada, Kanichiro, Satomi, Kazuhiko, Shinomiya, Kenichi,Tani, Toshikazu,. What Is the Best Multimodality Combination for Intraoperative Sinal Cord Monitoring of Motor Function? A Multicenter Study by the Monitoring Committee of the Japanese Society for Spine Surgery and Related Research. Global Spine J 2016;6(3):234-241.

(13) Pelosi L, Lamb J, Grevitt M, et al. Combined monitoring of motor and somatosensory evoked potentials in orthopaedic spinal surgery. *Clin Neurophysiol* 2002;113:1082–91.

(14) Pickell, M., Mann, S., Chakravertty, R., Borschneck,D. Surgeon-driven neurophysiologic monitoring in a spinal surgery population. Journal of Spine Surgery 2016;2(3).

(15) Calancie B, Harris W. "Threshold-level" multipulse transcranial electrical stimulation of motor cortex for intraoperative monitoring of spinal motor tracts: description of method and comparison to somatosensory evoked potential monitoring. - Journal of Neurosurgery (- 3):- 457.

(16) Bjerke B, Zuchelli D. Prognosis of Significant Intraoperative Neurophysiologic Monitoring Events in Severe Spinal Deformity Surgery. - Spine Deformity (- 2):- 117.

(17) Pajewski T, Arlet V. Current approach on spinal cord monitoring: the point of view of the neurologist, the anesthesiologist and the spine surgeon. - European Spine Journal (- Suppl 2):- 115.

(18) Vitale MG, Moore DW, Matsumoto H, Emerson RG, Booker WA, Gomez JA et al. Risk factors for spinal cord injury during surgery for spinal deformity. Journal of Bone and Joint Surgery - Series A. 2010 Jan 1;92(1):64-71.

(19) Gibson PR. Anaesthesia for correction of scoliosis in children. *Anaesth Intensive Care* 2004; 32:548–59

(20) Haghighi SS, Oro GG. Effect of hypovolemic hypotensive shock on somatosensory and motor evoked potentials. Neurosurgery 1989; 24: 246 ± 252.

(21) Salem, Khalid M. I., Goodger, Laura, Bowyer, Katherine, Shafafy, Masood, Grevitt, Michael P. Does transcranial stimulation for motor evoked potentials (TcMEP) worsen seizures in epileptic patients following spinal deformity surgery? Eur Spine J European Spine Journal 2016;25(10):3044-3048.

(22) DiCindio, Sabina, DO[*]; Theroux, Mary, MD[*]; Shah, Suken, MD[†]; Miller, Freeman, MD[†]; Dabney, Kirk, MD[†]; Brislin, Robert P., DO[*]; Schwartz, Daniel, PhD[‡] Multimodality Monitoring of Transcranial Electric Motor and Somatosensory-Evoked Potentials During Surgical Correction of Spinal Deformity in Patients With Cerebral Palsy and Other Neuromuscular Disorders, Spine: August 15, 2003 - Volume 28 - Issue 16 - p 1851-1855

(23) Iyer S, Nemani VM, Kim HJ. A Review of Complications and Outcomes following Vertebral Column Resection in Adults. *Asian Spine J*. 2016;10(3):601-609.

(24) Atici Y, Balioglu MB, Kargin D, Mert M, Albayrak A, Kaygusuz MA. Analysis of complications following posterior vertebral column resection for the treatment of severe angular kyphosis greater than 100°. Acta Orthopaedica et Traumatologica Turcica 2017 May 2017;51(3):201-208.

(25) Bridwell, Keith H., MD; Lenke, Lawrence G., MD; Baldus, Christy, LPN; Blanke, Kathy, RN Major Intraoperative Neurologic Deficits in Pediatric and Adult Spinal Deformity Patients: Incidence and Etiology at One Institution, Spine: February 1, 1998 - Volume 23 - Issue 3 - p 324-331

(26) Morris SH, Howard JJ, Rasmusson DD, El-Hawary R. Validity of transcranial motor evoked potentials as early indicators of neural compromise in rat model of spinal cord compression. *Spine (Phila Pa 1976)*. 2015;40(8):E492-E497.

Chapter 2

Publication ready manuscript

Abstract

Aims

Spinal deformity surgery carries the risk of neurological injury. Neurophysiological monitoring allows early identification of intraoperative cord injury facilitating early intervention which has a better prognosis.

Although multimodal monitoring is the ideal, resource constraints make surgeon directed intra-operative trans-cranial motor evoked potential (TcMEP) monitoring a useful compromise.

Our experience using surgeon directed TcMEP is presented in terms of viability, safety and efficacy.

Methods

A retrospective review was performed on a single surgeon's prospectively maintained database from 2010 to 2017 where TcMEP monitoring was utilised. The upper limbs were used as the control. A true alert was recorded when there was a 50% or more loss of amplitude of the lower limbs with maintained upper limb signals.

Patients with true alerts were identified and their case history analysed.

Results

Of the 299 cases were reviewed, 279 (93.3%) had acceptable traces throughout and awoke with normal clinical neurological function. No case with normal traces had a post-operative clinical neurological deficit.

True alerts occurred in 20 (6.7%) cases. The alert group diagnoses included adolescent idiopathic scoliosis 9 (45%) and congenital scoliosis 6 (30%). The incidence of deterioration based on diagnosis AIS was 9/153 (6%), congenital 6/30 (20%) and TB spine 2/16 (12.5%). Deterioration in congenital is much more common ($p=0.02$) when compared to AIS.

65% of alerts occurred during rod instrumentation and 15% during decompression of the internal apex in vertebral column resection surgery. 4 (20%) alert cases awoke with clinically detectable neurological compromise

Conclusion

Surgeon directed TcMEP monitoring has a 100% negative predictive value and allows early identification of physiological cord distress and immediate intervention.

In resource constrained environments, surgeon directed TcMEP is a viable and effective method of intra-operative spinal cord monitoring.

Clinical relevance

- Surgeon directed TcMEP monitoring has a 100% negative predictive value.
- In resource constrained environments, surgeon directed TcMEP is viable and effective
- Level 3 evidence

Manuscript

Introduction

Spinal deformity surgery carries a reported risk of neurological injury between 1.5% to 9%, climbing with complexity and congenital aetiology of the deformity [1, 2]. This neurological loss of function may be transient or permanent, the latter resulting in a devastating impact on the patient, their family and the surgeon.

Historically, intra-operative neurological assessment relied on the wake-up test and early post-operatively on the ankle clonus test. The wake-up test is challenging for the anaesthetist to wake the patient at the desired time, in a controlled manner without pain allowing active limb movement to command without the dangers of unintended extubation, loss of intravenous lines and patient recall. This also only provides an assessment at one moment in time when cord compression and resultant spinal cord injury may occur over minutes to even hours [3,].

Neurophysiological monitoring allows real time, repetitive or even continuous spinal cord function confirmation by a variety of methods to stimulate various neural tracts. It was first introduced in the early 1970s with monitoring of the sensory tracts by means of somatosensory evoked potentials (SSEP). By definition they only examine changes occurring in the ascending dorsal tracts of the spinal cord which may occur late in spinal cord injury (SCI). SSEP monitoring gives no direct indication of motor function and as a result has been documented to provide both false negatives and false positives. [4,5,6] SSEP monitoring and interpretation is complex and requires neurophysiologists to be present during the surgery which is labour intensive and a cost driver.

Motor evoked potentials (MEPs) were first described in 1980. [8] They directly monitor the descending motor tracts, the surgeons primary concern in spinal surgery. These are produced by synchronised excitatory volleys on corticospinal tracts and can be activated by cortical (transcranial) or direct spinal cord stimulation using either electrical or magnetic stimulation. The responses and signals are then monitored via needle electrodes placed sub dermally (neurogenic motor evoked potentials) or into muscles (myogenic evoked potentials). [7,9] Transcranial motor evoked potentials have been shown to have a sensitivity of 1.0, a specificity of 0.97, a negative predictive value of 1.0 and a positive predictive value of 0.67. [10] They are however far more sensitive to anaesthetic agents and require a total intravenous strategy avoiding muscle relaxants, volatiles and benzodiazepines which can be challenging for the anaesthetic staff.

The scoliosis research society issued a policy statement in 1992 advocating the use of neurophysiological monitoring to assist in early detection of complications and possibly prevent post-operative morbidity in patients undergoing spinal surgery. Neurophysiological monitoring is considered as a viable alternative and adjunct to the use of the wake-up test and ankle clonus test. [11]

Ideal spinal cord monitoring involves multimodal intra-operative monitoring using a combination of SSEP, MEP and electro-myelography (EMG). This provides the highest sensitivity and specificity with real time assessment. These require a well experienced team, specifically a neurophysiologist present throughout the procedure [12,13]. This is extremely labour intensive and with few available in South Africa, usually not possible.

In our resource constrained environment, it is difficult to justify this additional cost especially when most cases have normal electrophysiological status throughout. We have developed capacity to perform surgeon directed intra-operative trans-cranial motor evoked potential (TcMEP) monitoring using a simple setup of upper limbs as controls and lower limbs as the spinal cord assessment. [14]

The aim of this review was to present our experience using surgeon directed TcMEPs, assessing its viability, safety and efficacy.

Methods

A retrospective review was performed on a single surgeon's prospectively maintained database from 2010 to 2017. A consecutive 322 spinal deformity cases where TcMEP was employed was identified. Twenty-three cases were excluded as 16 had pre-existing neurological fallout, 6 had unobtainable traces and 1 was due to technical computer failure, leaving 299 consecutive cases.

The vast number of cases were adolescent idiopathic scoliosis (AIS) as per Table 1

Diagnoses for all cases	
Adolescent idiopathic scoliosis	153 (51.2%)
Neuromuscular scoliosis	51 (17.1%)
Congenital scoliosis	30 (10.0%)
Sagittal imbalance	17 (5.7%)
Post tuberculosis spine	16 (5.4%)
Degenerative spine with stenosis	14 (4.7%)
Non-union/ pseudarthrosis	11 (3.7%)
Dysplastic listhesis	4 (1.3%)
Tumour	3 (1.0%)

Table 1. Case diagnoses

Intra-operative monitoring

The Nim-Eclipse Spinal System (Medtronic) was used in all cases. Once the patient was asleep, transcranial corkscrew electrodes were placed on the vertex over the cortical motor strip in line with the ears a few centimetres either side of the midline. Needles were placed bilaterally in the thenar muscle bulk and medial to the 5th metacarpal, as well as in the feet medially inferior to the 1st metacarpal (abductor halluces) and subcutaneously on the dorsum. [9,12-17]

An effort to maintain the patient’s core temperature was made with external heating and avoiding body exposure where possible. Once the patient was fully anaesthetized, positioned, cleaned and draped a baseline stimulus run was initiated. The voltage was increased until good baseline upper and lower limb traces were observed. If this failed to yield good traces, the stimulation was doubled from a train of 4 to two trains of 4, the “double stim” option.[14,15,17] Care was taken to ensure the traces corresponded to the correct limbs, with arm signals occurring before leg signals, to confirm this.

Stimulus “runs” were then performed at specific high-risk points i.e. operating near the spinal cord, insertion of instrumentation, manipulation of spine with rod insertion and deformity correction, distraction and osteotomy.[14,16,18]

Although the literature reports physiological spinal cord distress when there is a TcMEP 50% loss of amplitude, or 10% increase in latency – this was not our experience. Intra-operatively there is significant signal volatility related to mean blood pressure (mBP), temperature and depth of anaesthesia. We relied on the relationship between upper and lower limb traces. When they dropped in unison, this was regarded as an anaesthetic issue and usually with increased mBP, they would improve, again in unison [9,10,12-17,].

We regarded discordant loss of lower limb traces with maintained upper limb traces as a true alert. The case notes for these true alerts were reviewed for pre-operative clinical status, intra-operative surgical events and physiological parameters, including mean blood pressure, hypothermia, blood loss, anaesthetic agents used and post-operative clinical findings and outcome.

When we encountered such a true alert, the surgeon would assess the last surgical step, and if appropriate undo it. This usually was removing a rod. Simultaneously the mBP would be raised and maintained above 75mmHg, both intra- and post-operatively.

No steroids were administered as the authors deem the NASCIS literature unconvincing of benefit over problems.

Should the traces return, correction would be continued, albeit less aggressively.

Neurological injury was defined as a detectable clinical change in motor or sensory assessment as compared to pre-operative examination.

Ethics approval was obtained from the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee and assigned as HREC REF: 785/2018.

Anaesthetic technique

Anaesthesia in spinal cord monitoring requires Total Intravenous Anaesthesia (TIVA) as anaesthetic vapours effect motor evoked potentials in a dose dependant manner. The choice of anaesthetic agents is based on the patients age and pre-existing co-morbidities. Target controlled infusion protocols are used to induce and maintain anaesthesia using weight adjusted dosages of propofol, sufentanil or remifentanil and dexmedetomidine, with the depth of anaesthesia being continuously monitored using the bispectral index monitor. The effects are titrated according to the various stages and demands of surgery to ensure the adequate maintenance of the required mean blood pressure and utilising vasopressors when indicated. Blood loss is further minimised by the administration of a tranexamic acid infusion intraoperatively. [19-22]

Results

In all 299 cases the surgeon completed the TcMEP monitoring process whilst operating. The screen was visible to the surgeon and he assessed the traces personally. The stimulation process was directed by the surgeon with the mouse operated by general theatre staff at his request.

279 (93.3%) cases had acceptable traces throughout and awoke with normal clinical neurological function. No case with normal traces had a clinical deficit.

True alerts occurred in 20 (6.7%) cases with an average age of 17years (12-52) with 50% male and 50% female.

The most common diagnosis in the alert group was adolescent idiopathic scoliosis (AIS) followed by congenital scoliosis. (Table 2.)

True alert group diagnoses	
AIS, severe progressive curve	45% (9)
Congenital Scoliosis	30% (6)
Post TB kyphoscoliosis	10% (2)
Post cardiac surgery, rigid	5% (1)
Neuromuscular	5% (1)
RA, chin on chest deformity	5% (1)

Table 2. True alert group diagnoses (TB; tuberculosis, RA; rheumatoid arthritis)

But when considering the incidence of deterioration based on diagnosis AIS was 9/153 (6%), congenital 6/30 (20%) and TB spine 2/16 (12.5%). This shows that deterioration in congenital is much more common (p=0.02) when compared to AIS.

Alerts occurred predominately during deformity correction usually with rod insertion. Of these 13 cases, 9 had traces return after reduction of the correction magnitude and/or release of distraction (Table 3.)

Alert events	
Correction, via rod instrumentation	13 (65%)
Vertebral column resection: decompression	3 (15%)
Iatrogenic injury	1 (5%)
Retraction, syrinx	1 (5%)
Screw, pedicle wall violation	1 (5%)
Neck extension	1 (5%)

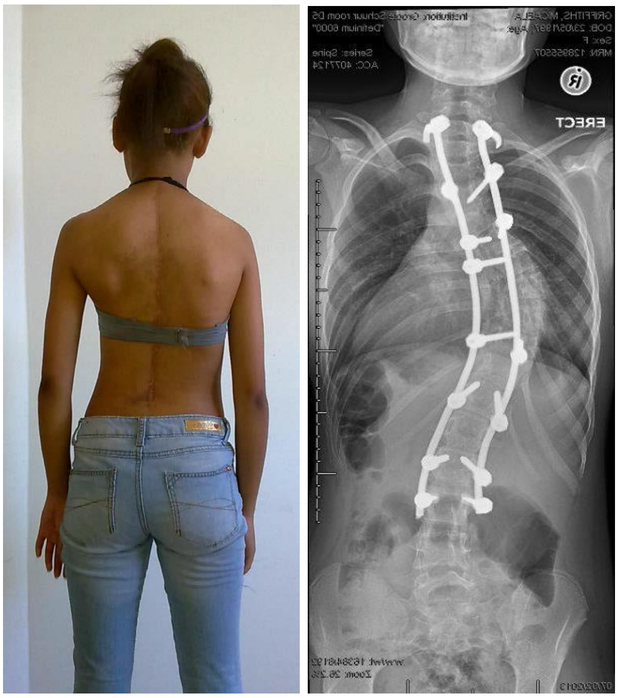
Table 3. Events at which alerts occurred

The remaining 4 cases required additional interventions as below.

In two cases although the rods were removed, the lower limb signal amplitudes remained low. All the screws were sequentially removed, pedicles probed and confirmed to be intact with no canal violations. The screws were replaced but not the rods. On waking, the patients had unilateral lower limb weakness. Post-operative MRI showed no cord oedema or signal. The patients subsequently had revision surgery 2 weeks later and rods replaced with a reduced correction and distraction. Both patients regained full power within days. (Figure 1.)

Figure1: Adolescent idiopathic scoliosis

Top: pre-operative clinical and x-ray images, Bottom: post-operative clinical and x-ray images



In the third case traces were lost after unilateral screw placement. These screws were then sequentially removed and probed and there were no pedicle wall violations noted. Reinsertion with stimulus runs after each screw showed a sub-alert drop in amplitude with placement of the apical screw on the concavity. This screw was then removed and re-probed and again no violation was noted. The screw was reinserted, and traces returned to baseline. On waking the patient was found to have a normal ankle clonus test and was moving both lower limbs. However, in the ward the patient slowly had unilateral progressive lower limb weakness. Further radiological investigation was not performed as the weakness corresponded with the intraoperative events. The case was taken to back to theatre and there was a finding of apical screw cut out and canal violation. The screw was removed, and rods replaced. The patient's neurological fallout recovered to normal

The fourth case had an alert recorded at wound closure. The wound was thus reopened, and the distraction and correction reduced resulting in a return of normal trace.

Other points of alerts were during the decompression phase of vertebral column resection (VCR) surgery, specifically whilst addressing the internal apex that compresses the cord in kyphotic deformities. (Figure2). The most devasting case had an alert during this phase and all traces were lost with no return at all for the duration of the procedure. The patient awoke with complete lower limb paralysis with no recovery. Two other VCR cases had similar alerts but awoke with the same neurological state as preoperatively.

One alert occurred during manipulation of the head clamp to correct a cervical kyphosis with chin on chest deformity. This returned with re-adjustment of the cervical position.

Pedicle wall violation with an apical screw accounted for one alert and another alert occurred from retraction over a syrinx. An iatrogenic induced alert occurred when the Kerrison slipped onto the exposed spinal cord resulting in a durotomy that was repaired, and the patient awoke with no neurological fallout.

Figure 2. Pre-operative lateral x-ray in congenital scoliosis

Severity of curves

The cobb angles measured in the alert group cases diagnosed with AIS had a mean of 102.01 degrees with a maximum of 122 degrees and a minimum of 70.2 degrees.

The kyphotic angles in those diagnosed with congenital scoliosis and post tuberculosis kyphosis ranged from 49.2 degrees to a maximum of 121 degrees with a mean of 84.64 degrees

Discussion

Neurological injury is a devastating risk of spinal deformity surgery. With more sophisticated implants and aggressive correction techniques available, larger, stiffer curves are addressed with more correction than in the past. Early recognition of spinal cord distress is imperative to allow rectifying action to prevent progression to clinical neurological functional loss. From animal models it appears one has about 5 minutes before this occurs [23].

Neurological injury is far higher as the curve becomes larger and more rigid. Kyphotic associated deformities, especially when rigid, are the highest risk reported up to 35% when VCR is employed.[24,25] In these cases, the spinal cord is stretched and often flattened over the apical internal vertebral body ("internal gibbus") resulting in a cord that is predisposed to insult. It is our experience alerts occurred with minimal insult or manipulation.

Bridwell et al reports that cord injury in deformity surgery may be from mechanical compression, cord distraction, pure vascular insult or a combination of all 3. [26]. They confirm our experience with most alerts occurring during deformity correction via rod instrumentation, when the spinal cord is at risk of tension as the spinal column is lengthened.

We experienced events with rotational and coronal correction, but more so with sagittal correction from a kyphotic position and distraction when balancing. As alerts did not occur in 93% of our cases with the same techniques, it is not the technique itself but rather the specific patient's cord vulnerability. The AIS curves tended to be of large magnitude, less flexible in older patients but not always the case. Again, many such curves did not have alerts. Typically, congenital scoliosis is rigid and has a kyphotic element. Correction may occur over a more focal point rather than evenly spread over the whole curve such as a flexible AIS. To our mind, this adds to the risk.

With VCR surgery, there is much higher risk. In our experience there is often pre-operative cord distress with at least brisk reflexes or tone changes. The procedure itself with the total disconnection of the spinal column allows inadvertent translation and cord tension during the correction process, which despite all efforts by the surgical team, is not always controlled throughout the process.

Anaesthetic control is all important. The correction is usually occurring after a prolonged period of surgery, especially in VCR / osteotomy surgery, where there may have been significant blood loss and a volatile blood pressure. Sadly, this component is often sub-optimal in our environment with ever changing staff especially in a teaching hospital. They need to be actively involved at all stages maintaining a steady mean blood pressure (mBP), we request over 75mmhg as a compromise between bleeding, visualisation and cord perfusion. This is often dictated by the amplitude of the TcMEPs where is both upper (control) and lower limb traces are low, we ask for a higher mBP.

Educating our anaesthetists and obtaining compliance with protocols was challenging as was creating a bidirectional communication environment to correlate autonomic suggestions of trouble and TcMEPs. The adoption of total intravenous anaesthesia and the interplay between all the drugs was stressful, particularly with prolonged waking up times after the procedure to confirm normal spinal cord function. Unfortunately, this seems to be a learning curve with the typical models not always predictive in our challenging patient group.

Acute spinal cord injury usually manifests with initial acute hypertension (thus the need for real time arterial monitoring) and tachycardia which is then followed by hypotension. The anaesthetic team needs to be vigilant as all too often one finds them supporting the patient with vasoconstrictors without saying a word, in the belief the patient is behind on fluids.

As TcMEPs are run on demand rather than continuously, one needs to know whenever there is any autonomic change so a “run” can be initiated to confirm cord physiological function.

In our experience, once there was lower limb signal loss with correction, and return after a few minutes with rod removal, subsequent attempts at correction resulted in repetitive signal loss despite lesser attempt at correction. It appeared that once there was physiological cord distress, it became sensitised to tension. Thus, in these cases, the rods were left out, but screws left in and the patient closed. These patients usually had transient mild neurological impairment from paraesthesia to some weakness which rapidly resolved over hours to 1-2 days. Post-op MRI did not confirm a cord signal despite the clinical picture.

These patients were taken back about 2 weeks later where the rods were re-inserted with reasonable correction and better than the signals allowed at the index surgery. This suggests physiological recovery of the cord to a less vulnerable state

In our resource restricted environment there is no neurophysiologist available for theatre monitoring in the public sector and only one in the local private sector. In the so-called “first world” this is not the case and trained specialist neurologists may even monitor. Although utopian, this cost driver is often questioned especially with the relatively low incidence of problems in “routine” deformity cases such as AIS. This has led to less than ideal remote monitoring solutions where a neurophysiologist monitors multiple cases simultaneously via the internet. Locally technicians may be utilised in the private sector, but they are not licenced to interpret the signals. Unknowingly the surgeon is taking responsibility without realising it.

It is our view that to maximise the benefits of SCM, the team must be in constant communication regarding the stage of procedure, current cord risk, autonomic state of the patient and the SCM output on the screen. The ideal is to have a neurophysiologist in theatre but where this is not possible, TcMEPs can be employed by a surgeon who has acquired the requisite insights as to waveform interpretation, especially in the case of loss of signals to confirm whether in fact they are real or artefactual.

We have successfully employed a simple TcMEP monitoring set-up using 4 channels, two hands and two legs. The hand signals act as a control in the setting of thoracic surgery where their presence confirms a working system. Should they remain unchanged and there is loss of the leg signals, there is thoracic cord distress.

The literature suggests percentage amplitude changes as indications of cord distress. In our view this is less useful than constantly comparing the amplitude of the hand and legs. Should both fall by 50%, it indicates an anaesthetic issue – usually falling mBP or hypothermia. If this mBP fall was slow and steady it is usually a fluid balance issue and the traces respond to anaesthetic intervention. When we experienced loss of leg signals with maintained hand signals, it was usually close to or total loss. TcMEPs seem to behave in a categorical manner.

Despite the alerts, the vast majority of our patients awoke with normal neurological function with only 4 (20%) having a clinical deficit. This begs the argument of whether the alert was “real” or not. TcMEPs are extremely sensitive and change seems to precede clinical fall out. We believe this offers the surgeon an opportunity to intervene early. Of course, one does not know what the clinical scenario would be if you did not intervene with signal loss, but this is a risk most of us would not take.

In the end, if you use SCM you must believe it. As all our patients with normal TcMEPs had normal clinical neurological status, this technique offers the surgeon very welcome reassurance whilst stressed performing complex surgery. This is particularly reassuring when patients take hours to wake or need to be kept intubated overnight for other reasons.

Other than one patient with transient hair loss around the stimulation electrodes there were no adverse effects of the TcMEPs.

Conclusion

Surgeon directed TcMEP spinal cord monitoring is a viable option. It allows safer surgery in environments where there is poor neurophysiologist support and a cost-saving consideration in routine cases with very low alert incidence, such as AIS, in the developed world.

It has a 100% negative predictive value as no patient with normal intra-operative traces had post-operative neurological deficit which is a massive reassurance to the surgeon.

As it provides real time spinal cord status, it allows immediate intervention by the surgeon should an alert occur, usually with favourable outcome.

References

1) MacEwen GD, Bunnell WP,Sriram K. Acute neurological complications in the treatment of scoliosis. A report of the Scoliosis Research Society. The Journal of bone and joint surgery. American volume 1975;57(3):404-8.

(2) Weiss HR GD. Rate of complications in scoliosis surgery - a systematic review of the Pub Med literature. Scoliosis 2008;3.

(3) Hoppenfeld S, Gross A, Andrews C, Lonner B. The ankle clonus test for assessment of the integrity of the spinal cord during operations for scoliosis. The Journal of bone and joint surgery. American volume 1997;79(2):208-12.

(4) Padberg AM, Wilson-Holden T, Lenke LG, Bridwell KH. Somatosensory and Motor Evoked Potential Monitoring Without a WakeUp Test During Idiopathic Scoliosis Surgery: An Accepted Standard of Care. Spine 1998;23(12).

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

(6) Lesser RP, Raudzens P, Lüders H, et al. Postoperative neurological deficits may occur despite unchanged intraoperative somatosensory evoked potentials. *Ann Neurol*1986;19:22–5

(7) Macrì S, De Monte A, Greggi T, Parisini P, Zanoni A, Merlini L. Intra-operative spinal cord monitoring in orthopaedics. Spinal Cord 2000 03;38(3):133.

(8) Merton PA, B Morton ,H. Stimulation of the Cerebral Cortex in the Intact Human Subject. ; 1980.

(9) Luk KD, Hu Y, Wong YW, et al. Evaluation of various evoked potential techniques for spinal cord monitoring during scoliosis surgery. *Spine* 2001;26:1772–7

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

(11) Scoliosis Research Society position statement. Somatosensory evoked potential monitoring of neurologic spinal cord function during spinal surgery. Scoliosis Research Society, Kansas City, Missouri, September 1992.

(12) Ito, Zenya, Matsuyama, Yukihiro, Ando, Muneharu, Kawabata, Shigenori, Kanchiku, Tsukasa, Kida, Kazunobu, Fujiwara, Yasushi, Yamada, Kei, Yamamoto, Naoya, Kobayashi, Sho, Saito, Takanori, Wada, Kanichiro, Satomi, Kazuhiko, Shinomiya, Kenichi,Tani, Toshikazu,. What Is the Best Multimodality Combination for Intraoperative Sinal Cord Monitoring of Motor Function? A Multicenter Study by the Monitoring Committee of the Japanese Society for Spine Surgery and Related Research. Global Spine J 2016;6(3):234-241.

(13) Pelosi L, Lamb J, Grevitt M, et al. Combined monitoring of motor and somatosensory evoked potentials in orthopaedic spinal surgery. *Clin Neurophysiol* 2002;113:1082–91.

(14) Pickell, M., Mann, S., Chakravertty, R., Borschneck,D. Surgeon-driven neurophysiologic monitoring in a spinal surgery population. Journal of Spine Surgery 2016;2(3).

(15) Calancie B, Harris W. “Threshold-level” multipulse transcranial electrical stimulation of motor cortex for intraoperative monitoring of spinal motor tracts: description of method and comparison to somatosensory evoked potential monitoring. - Journal of Neurosurgery (- 3):- 457.

(16) Bjerke B, Zuchelli D. Prognosis of Significant Intraoperative Neurophysiologic Monitoring Events in Severe Spinal Deformity Surgery. - Spine Deformity (- 2):- 117.

(17) Pajewski T, Arlet V. Current approach on spinal cord monitoring: the point of view of the neurologist, the anesthesiologist and the spine surgeon. - European Spine Journal (- Suppl 2):- 115.

(18) Vitale MG, Moore DW, Matsumoto H, Emerson RG, Booker WA, Gomez JA et al. Risk factors for spinal cord injury during surgery for spinal deformity. Journal of Bone and Joint Surgery - Series A. 2010 Jan 1;92(1):64-71.

(19) Gibson PR. Anaesthesia for correction of scoliosis in children. *Anaesth Intensive Care* 2004; 32:548–59

(20) Haghighi SS, Oro GG. Effect of hypovolemic hypotensive shock on somatosensory and motor evoked potentials. Neurosurgery 1989; 24: 246 ± 252.

(21) Salem, Khalid M. I., Goodger, Laura, Bowyer, Katherine, Shafafy, Masood, Grevitt, Michael P. Does transcranial stimulation for motor evoked potentials (TcMEP) worsen seizures in epileptic patients following spinal deformity surgery? Eur Spine J European Spine Journal 2016;25(10):3044-3048.

(22) DiCindio, Sabina, DO[*]; Theroux, Mary, MD[*]; Shah, Suken, MD[†]; Miller, Freeman, MD[†]; Dabney, Kirk, MD[†]; Brislin, Robert P., DO[*]; Schwartz, Daniel, PhD[‡] Multimodality Monitoring of Transcranial Electric Motor and Somatosensory-Evoked Potentials During Surgical Correction of Spinal Deformity in Patients With Cerebral Palsy and Other Neuromuscular Disorders, Spine: August 15, 2003 - Volume 28 - Issue 16 - p 1851-1855

(23) Morris SH, Howard JJ, Rasmusson DD, El-Hawary R. Validity of transcranial motor evoked potentials as early indicators of neural compromise in rat model of spinal cord compression. *Spine (Phila Pa 1976)*. 2015;40(8):E492-E497.

(24) Iyer S, Nemani VM, Kim HJ. A Review of Complications and Outcomes following Vertebral Column Resection in Adults. *Asian Spine J*. 2016;10(3):601-609.

(25) Atici Y, Balioglu MB, Kargin D, Mert M, Albayrak A, Kaygusuz MA. Analysis of complications following posterior vertebral column resection for the treatment of severe angular kyphosis greater than 100°. Acta Orthopaedica et Traumatologica Turcica 2017 May 2017;51(3):201-208.

(26) Bridwell, Keith H., MD; Lenke, Lawrence G., MD; Baldus, Christy, LPN; Blanke, Kathy, RN Major Intraoperative Neurologic Deficits in Pediatric and Adult Spinal Deformity Patients: Incidence and Etiology at One Institution, Spine: February 1, 1998 - Volume 23 - Issue 3 - p 324-331