The Spine Journal 19 (2019) 377−385

Clinical Study

The reliability of motor evoked potentials to predict dorsiflexion injuries during lumbosacral deformity surgery: importance of multiple myotomal monitoring

Jeremy A. Lieberman, MD[a,*], Russ Lyon, PhD, DABNM[b], Paul Jasiukaitis, PhD, CNIM[b], Sigurd H. Berven, MD[c], Shane Burch, MD[c], John Feiner, MD[a]

[a] *Department of Anesthesia & Perioperative Care, University of California, San Francisco, San Francisco, CA 94143, USA*
[b] *Division of Operating Room Services, University of California, San Francisco, San Francisco, CA 94143, USA*
[c] *Department of Orthopedic Surgery, University of California, San Francisco, San Francisco, CA 94143, USA*
Received 26 March 2018; revised 8 July 2018; accepted 9 July 2018

Abstract

STUDY DESIGN: Case-control analysis of transcranial motor evoked potential (MEP) responses and clinical outcome.

OBJECTIVE: To determine the sensitivity and specificity of MEPs to predict isolated nerve root injury causing dorsiflexion weakness in selected patients having complex lumbar spine surgery.

SUMMARY OF BACKGROUND DATA: The surgical correction of distal lumbar spine deformity involves significant risk for damage to neural structures that control muscles of ankle and toe dorsiflexion. Procedures often include vertebral translation, interbody fusion, and posterior-based osteotomies. The benefit of using MEP monitoring to predict dorsiflexion weakness has not been well-established. The purpose of this paper is to describe the relationship between neural complications from lumbar surgery and intraoperative MEP changes.

METHODS: Included were 542 neurologically intact patients who underwent posterior spinal fusion for the correction of distal lumbar deformity. Two myotomes, including tibialis anterior (TA) and extensor hallucis longus (EHL), were monitored. MEP and free-running electromyography data were assessed in each patient. Cases of new dorsiflexion weakness noted postoperatively were identified. Data in case and control patients were compared. There was no direct funding for this work. The Department of Anesthesiology and Perioperative Care provides salary support for authors one and six. Authors two and three report employment in the field of intraoperative neurophysiological monitoring as a study-specific conflict of interest.

RESULTS: Twenty-five patients (cases) developed dorsiflexion weakness. MEP amplitude decreased in the injured myotomes by an average of 65 ± 21% (TA) and 60±26% (EHL), which was significantly greater than the contralateral uninjured side or for control subjects. ($p < .01$) Receiver operator characteristic (ROC) curves showed high sensitivity, specificity, and predictive

FDA device/drug status: Approved (Digitimer D-185 stimulator and Cadwell TCS-4 stimulator).

Author disclosures: ***JL***: Consulting: Medtronic ($0); Grants: University of California, San Francisco (D, University funded competitive grant to support basic research involving spine surgery). ***RL***: Nothing to disclose. ***PJ***: Nothing to disclose. ***SHB***: Royalties: Stryker (F); Stock Ownership: Providence Medical (1%), Globus Medical (1%); Private Investments: Green Sun Medical (1%); Consulting: Medtronic (C); Speaking and/or Teaching Arrangements: Medtronic (B), Stryker Spine (C), Globus (B); Trips/Travel: Scoliosis Research Society (Financial, Payment for Travel and Hotel for Cabinet meeting, Paid directly to institution/employer); Board of Directors: Stryker Spine (Nonfinancial); Scientific Advisory Board: Globus Medical (Financial, Stock options); Grants: AO Spine (E, Fellowship Support, Paid directly to institution/employer), Globus (D, Fellowship support, Paid directly to institution/employer); Fellowship Support: Globus Medical (D, Fellowship Support). ***SB***: Consulting: MEDTRONIC (C); Speaking and/or Teaching Arrangements: Medtronic (D), MISONIX, Inc. (B), Zimmer Biomet (B); Grants: MISONIX, Inc. (A); Fellowship Support: NuVasive (D, Fellowship Support, Paid directly to institution/employer), Globus (E, Fellowship Support, Paid directly to institution/employer), AOSpine (D, Fellowship Support). ***JF***: Nothing to disclose.

Funding: UCSF Dept. of Anesthesia & Perioperative Care.

The disclosure key can be found on the Table of Contents and at www.TheSpineJournalOnline.com.

* Corresponding author. Department of Anesthesia & Perioperative Care, UCSF, Box 0648, 4th Floor, Millberry Union, East Tower, Room MUE-413, 500 Parnassus Avenue, San Francisco, CA 94143, USA. Tel.: +94143-0648.

E-mail address: jeremy.lieberman@ucsf.edu (J.A. Lieberman).

https://doi.org/10.1016/j.spinee.2018.07.006
1529-9430/

value for changes in MEP amplitude using either the TA or EHL. Analysis of MEP changes to either TA or EHL yielded a superior ROC curve. Net reclassification improvement analysis showed assessing MEP changes to both TA and EHL improved the predictability of injury.

CONCLUSIONS: The use of MEP amplitude change is highly sensitive and specific to predict a new postoperative dorsiflexion injury. Monitoring two myotomes (both TA and EHL) is superior to relying on MEP changes from a single myotome. Electromyography activity was less accurate but compliments MEP use. Additional studies are needed to define optimal intraoperative MEP warning thresholds.

Keywords: Electromyography; Foot drop; Lumbar deformity; Motor evoked potentials; Nerve root injury; Pedicle subtraction osteotomy; Spondylolisthesis.

Introduction

Loss of dorsiflexion strength, that is, "foot drop" injuries, may occur during lumbar surgery as a result of damage to spinal nerve roots. The muscles responsible for ankle and toe dorsiflexion are primarily innervated by the L5 nerve root, with L4 and S1 also contributing some innervation [1,2]. Damage to L5 occurs more often than any other lumbar nerve root [3]. L5 injury after high-grade L5−S1 spondylolisthesis reduction has been reported to be as high as 45%, but the range is quite variable [4−8]. Distal lumbar nerve root injury is also a frequent complication after transforaminal lumbar interbody fusion (TLIF [9]) and lumbar pedicle subtraction osteotomy (PSO) [10,11].

Intraoperative neurophysiological monitoring has been used to detect and prevent neural injury during spine surgery [12]. When focusing solely on lumbar spine nerve roots, prior literature on electromyography (EMG) has demonstrated high sensitivity to detect nerve root trauma [13,14]. However, recent studies challenge this assertion, with the sensitivity of EMG to detect isolated nerve root injury ranging from 0% to 60%, at best [15,16]. In animal studies using direct retraction or compression of a nerve root, EMG activity was often absent despite marked loss of nerve function [17,18]. Somatosensory evoked potentials have also been shown to have limited efficacy for detecting an isolated nerve root injury [19−22].

Transcranial motor evoked potential (MEP) monitoring has remained controversial as a technique to follow the integrity of individual spinal nerve roots. Animal studies have shown that MEPs are both highly sensitive and specific for predicting injuries. Sequential transection of nerve roots produced reproducible MEP amplitude decreases in swine [23]. Sustained retraction and compression of isolated nerve roots produced similar reductions to MEP amplitude [17,18]. Clinical studies have shown that MEP monitoring is effective for detecting nerve root injury in humans during spinal deformity correction, but only a small number of cases are described [10,24−26]. The purpose of this study is to report the reliability of motor evoked potentials using multiple myotomes to predict postoperative dorsiflexion strength loss during deformity surgery involving the lumbosacral spine in a relatively large cohort of injured patients.

Methods

Patient selection

After obtaining approval from the Committee on Human Research, we retrospectively studied patients who underwent posterior spinal fusion for correction of lumbosacral deformity from 2009 to 2014. All procedures were performed in the prone position, though some patients had additional anterior or lateral operations.

The primary surgical team obtained a baseline neurologic assessment before surgery and performed a postoperative exam as soon as the patient was alert enough to cooperate after the procedure was complete. Motor strength was based on a standard 0−5 scale. Dorsiflexion injury was defined as any decrease in motor strength observed when trying to dorsiflex the whole foot (tibialis anterior [TA] strength) or the large toe (extensor hallucis longus [EHL] strength). A change, even less than one full motor grade, was considered a meaningful difference from baseline.

We only included patients who had intraoperative MEP monitoring of both the TA and EHL muscles. We excluded patients with pre-existing motor deficits in either the TA or EHL; that is, the motor score was 5/5 at baseline for both of these myotomes bilaterally in all subjects.

Anesthesia

All operations were performed under general anesthesia. The regimen was not standardized but was designed to allow for evoked potential monitoring. In all patients, the core anesthetic consisted of infusions of propofol and an opioid. Additional infusions of ketamine and/or lidocaine were used at the discretion of the anesthesiologist. Inhaled volatile anesthetic gases were sometimes used, but it was always limited to $\leq$0.3 MAC and was removed if MEP signals were initially weak or were fading [27]. Neuromuscular blockade was used only to facilitate intubation. Complete recovery was confirmed before obtaining baseline MEP responses.

Neurophysiologic monitoring

All patients were monitored with spontaneous EMG and with multimyotomal motor evoked potentials. Somatosensory evoked potential monitoring was added if the surgery extended up to L1 or higher, for enhanced monitoring of the spinal cord.

Multipulse transcranial electrical stimulation was generated with either a Digitimer D-185 constant-voltage stimulator (Digitimer LTD, Welwyn Garden City, UK) or a Cadwell TCS-4 (Cadwell Laboratories, Inc., Kennewick, WA, USA). The stimulator produced one to nine pulses at a fixed duration of 50 ms with an Interstimulus Interval that was adjusted between 1 and 4 ms. Stimuli were delivered through 2 ''corkscrew'' stimulating electrodes (Nicolet Biomedical, Inc., Memphis, TN, USA) placed at the standardized 10−20 electrode positions of C1 and C2, which overlie the motor cortex. The stimulator interfaced with the electrophysiological recording platform (Cadwell Cascade/Elite, Cadwell Laboratories, Inc., Kennewick, WA, USA) so that a ''triggered'' EMG response was elicited with each stimulus. Recording and filtering parameters were typically 30−1,000 Hz, at a time base of 100 ms. EMG activity evoked by transcranial stimulation was recorded using subdermal needle electrodes (Medtronic-Xomed, Rochester, MN, USA), which were placed approximately 4−6 cm apart in the rectus femoris, TA, EHL, and the foot flexor (FF) muscles of the bilateral lower extremities in all patients. To specifically assess dorsiflexion, the TA electrodes were typically placed in the TA at midcalf. The EHL electrodes were located in the distal third segment of the EHL muscle, about two to three finger-breaths proximal to the ankle, just lateral to the TA tendon insertion. Occasionally, we monitored additional myotomes, including the adductor longus, gastrocnemius, vastus lateralis, and/or vastus medialis.

Intraoperatively, a significant change in MEP responses that elicited a warning to the surgeon was determined by the clinical neurophysiologist. This was typically defined as an amplitude decrease of ≥80% from baseline in any myotome. Spontaneous EMG activity was recorded using the same recording myotomes as for MEP responses. If one observed neurotonic discharges lasting longer than 5 seconds, this elicited an MEP trial. We defined "significant" EMG findings as the above activity that was associated with concurrent MEP amplitude changes [28].

Data analysis and statistics

The primary outcome was the presence of dorsiflexion weakness of either the whole foot or large toe during the initial postoperative motor exam. This exam was performed by a spine surgeon within 1−2 hours after emergence from anesthesia, typically while in the PACU. Six patients with injury were admitted directly to the ICU. Four were extubated in the OR and early exams performed. Two remained intubated on admission and the exams were performed within 12 hours of the end of surgery. We selected 50 uninjured patients from our cohort to serve as controls for the 25 injured patients. We analyzed the sensitivity of motor evoked potentials to predict weakness using a case-control comparison.

Foot drop injury cases and controls were compared by Wilcoxon rank sum for continuous variable, and Fisher's exact test for gender. Data are summarized by mean ± SD or number (percent). Motor evoked potentials, drop in potential, and motor strength are summarized as median (interquartile range). Comparison of control, case injured, and case uninjured were by the Kruskal-Wallis test and chi-square test. Lack of difference in the baseline MEPs of the injured and uninjured sides of cases were confirmed by the Wilcoxon sign rank test.

The last three MEP trials were averaged together to serve as the final amplitude for analysis. Receiver operator characteristic (ROC) curves were generated for the percent drop in motor evoked potential amplitude vs presence of weakness. Data for each side were considered as individual data points. The area under the curve (AUC) with 95% confidence intervals (CI) was calculated. ROC curves were for the different monitored muscles were compared statistically. Sensitivity, specificity, positive, and negative predictive values for different thresholds of the drop in motor evoked potential were calculated for determination of muscle weakness.

In cases with the area under the ROC curve are high, it can be difficult to show improvement in prediction values by using changes in multiple muscles rather than a single muscle, since the 95% CI overlap. We calculated the net reclassification improvement (NRI) of predicting injury when using two muscles that produce dorsiflexion (the TA and the EHL). We assessed both the event NRI and nonevent NRI [29]. If the first muscle group showed a positive MEP amplitude drop, we did not consider that a larger decline in MEP in the second muscle changed the classification. However, if the drop in MEP amplitude was smaller than that of the first muscle group, this could result in a reclassification to a true positive if there was weakness (upward event reclassification) or a false positive if there was no weakness (downward nonevent reclassification).

A p value $< .05$ was considered statistically significant. Data were analyzed with Stata 14.2 (StataCorp, College Station, TX, USA) and Microsoft Excel for Mac 2011 version 14.4.6 (Microsoft Corporation, Redmond, WA, USA).

Results

Between the years 2009 and 2014, we identified 542 patients at our institution without pre-existing dorsiflexion weakness that underwent posterior spinal fusion for lumbar deformity using intraoperative MEP monitoring. Twenty-five patients (4.6%) developed new dorsiflexion weakness on their initial postoperative motor exam as compared with baseline (Table 1). Injury rates were highest among patients who underwent reduction of high-grade L5−S1 spondylolisthesis (Meyerding Class 3+ [30]) or had a PSO; 8.2% and 7.5%, respectively. Twenty-four of the 25 foot drop injuries were unilateral, 12 on the right side and 12 on the left side. One patient was noted to have new bilateral weakness. Nine patients were noted to have severe weakness, defined

Table 1
Demographic information for posterior lumbar spinal fusion patients. Cases are patients noted to have weakness on initial postoperative neurologic examination

Patients for MEP analysis:	Control		Case	All	p value
n	50 (66.7%)		25 (33.3%)	75 (100.0%)	
Age (years)	60 ± 13		54 ± 21	58 ± 16	.63
Gender					.09
Female	23 (46.0%)		17 (68.0%)	40 (53.3%)	–
Male	27 (54.0%)		8 (32.0%)	35 (46.7%)	–
Weight (kg)	78.3 ± 18.0		80.9 ± 23.2	79.1 ± 19.7	.62
Height (cm)	167 ± 12		165 ± 13	166 ± 12	.22
BMI (kg/m^2)	27.9 ± 5.4		29.3 ± 4.6	28.3 ± 5.1	.16
	Controls	Cases - All	Cases - Severe (<3/5)	Total cohort	p value (control vs case)
n	50	25	9	542	
Procedure					.55
HG Spondylolisthesis reduction	11 (22.0%)	7 (28.0%)	1 (4.0%)	85 (15.7%)	
PSO − L4 or L5	14 (28.0%)	9 (36.0%)	3 (12.0%)	120 (22.1%)	
TLIF	12 (24.0%)	6 (24.0%)	3 (12.0%)	140 (25.8%)	
Other	13 (26.0%)	3 (12.0%)	2 (8.0%)	197 (36.3%)	

Data are mean ± SD, or n (%).
HG, high-grade; PSO, pedicle subtraction osteotomy; TLIF, transforaminal lumbar interbody fusion; BMI, body mass index.

as loss of antigravity strength (<3/5). Nerve injury cases did not differ from controls in age, gender, weight, height, BMI, or type of surgery (Table 1).

The precise moment during surgery when injury occurs cannot be known. We estimate the time of injury to occur proximate to a significant reduction in MEP amplitude that fails to improve with intervention. In our study, all seven injured high-grade spondylolisthesis patients had MEP amplitude changes between 14 and 55 minutes after reduction of the spondylolisthesis. Seven of the nine injuries in the PSO group occurred after closure of the osteotomy (five after L5 PSO; two after L4 PSO). Two other injuries occurred during the decompression phase and were associated with dural tears. Six patients who underwent TLIF were injured, four during nerve retraction while performing the discectomy and two others during TLIF cage placement. The remainder of MEP changes associated with injuries were observed during correction of lumbar deformities or during Smith-Petersen osteomies.

Significant EMG activity, as previously defined, was observed in 10 (40%) of the injured patients. Reproducible bilateral baseline MEP responses in the TA and EHL were obtained from all patients who sustained injury and from all 50 control patients, selected from the uninjured patient cohort. Baseline potentials did not differ for the TA or EHL (Table 2). Baseline potential for the injured and uninjured side were not different when compared by the Wilcoxon sign rank test (p values = .35 and .84 for TA and EHL respectively). Examples of intraoperative MEP changes that were associated with new foot drop injuries are shown in Fig. 1. The mean MEP amplitude decrease from baseline for patients with any dorsiflexion injury was 67 ± 21% in the TA and 65 ± 26% in the EHL. This was significantly different from their contralateral (uninjured) side and from the control group, where there were minimal changes from baseline. (p < .01) For severe injury (<3/5), the mean decrease in MEP amplitude for the TA and EHL were 75 ± 25% and 76 ± 17%, respectively. (p < .05 vs MEP decrease for any weakness present).

ROC curves relating amplitude changes to motor injury are shown in Fig. 2. The AUC for both rectus femoris and foot flexors (FFL) were significantly lower, and are shown as a negative control. The AUC for TA drop (0.94, 95%CI: 0.89−0.97) and EHL (0.95, 95%CI: 0.91−0.98) were similar. Utilizing the MEP amplitude change in either muscle (TA and/or EHL) resulted in a better AUC (0.99, 95%CI: 0.95−1.00). Using NRI analysis, the addition of a second myotome did improve the accuracy of MEP changes to predict injury compared with relying on MEP changes to either myotome alone. NRI is summarized in Table 3, showing up to a 26.9% improvement depending on the threshold for the drop in motor evoked potential. Not surprising, at lower thresholds, most reclassifications were downward (new false positives). However, at higher thresholds, additional true positives were detected (upward reclassification) without significant addition of false positives.

When assessing the larger MEP decrease of either the TA or EHL, the average MEP amplitude decreased by 72 ± 17% for any observed injury and 84 ± 12% for severe injury (<3/5). Detailed summaries of sensitivity, specificity and predictive values relative to degree of weakness are shown in Table 4. MEP amplitude decrease of 50% yielded the greatest accuracy while maintaining near maximal sensitivity for all injuries; MEP decrease of 60% produced optimal accuracy for severe injury (<3/5).

Discussion

Surgeons rely on intraoperative monitoring to help guide intraoperative decisions that might prevent a neurologic injury. Electrophysiological changes must be of sufficiently

Table 2
Summary of motor evoked potentials in controls and cases with nerve injury

Muscle group n	Control 100	Case: uninjured 24	Case: weak 26
Tibialis anterior			
Baseline (μV)	644 (412−982)	463 (273−1,006)	820 (193−1,063)
Final (μV)	580 (374−900)	426 (272−986)	157 (54−419) †
Percent drop	13.6% (−17.7% to 29.5%)	6.4% (−15.5% to 18.5%)	67.1% (46.5% to 82.9%) *
Final strength	5.0 (5.0−5.0)	5.0 (5.0−5.0)	4.0 (3.0−4.0)
Weakness	0 (0.0%)	0 (0.0%)	26 (100.0%)
Extensor hallucis longus			
Baseline (μV)	514 (335−797)	420 (283−564)	516 (199−772)
Final (μV)	496 (331−854)	411 (225−543)	144 (61−291) †
Percent drop	7.0% (−17.1% to 17.1%)	−6.2% (-25.6% to 14.1%)	64.7% (59.9%−72.7%) *
Final strength	5.0 (5.0−5.0)	5.0 (5.0−5.0)	3.3 (2.1−4.0)
Weakness	0 (0.0%)	0 (0.0%)	22 (100.0%)

Data are median (interquartile range), or n (%). Data are for 2 sides in 50 controls and 25 cases.
Comparisons by Wilcoxon rank sum or Fisher's exact test.
† p < 0.001 vs baseline amplitude.
* p < 0.001 vs both uninjured side and control.

high sensitivity so as to not miss a new injury (eg, no false negatives). In addition, effective monitoring should also maintain high specificity, as false positive alerts are disruptive. Surgeons have historically relied on mechanically-elicited EMG, believing it to be dependable and accurate [13,14]. However, recent examples in both the clinical and animal literature suggest that mechanically-elicited EMG exhibits a lower degree of sensitivity and specificity to

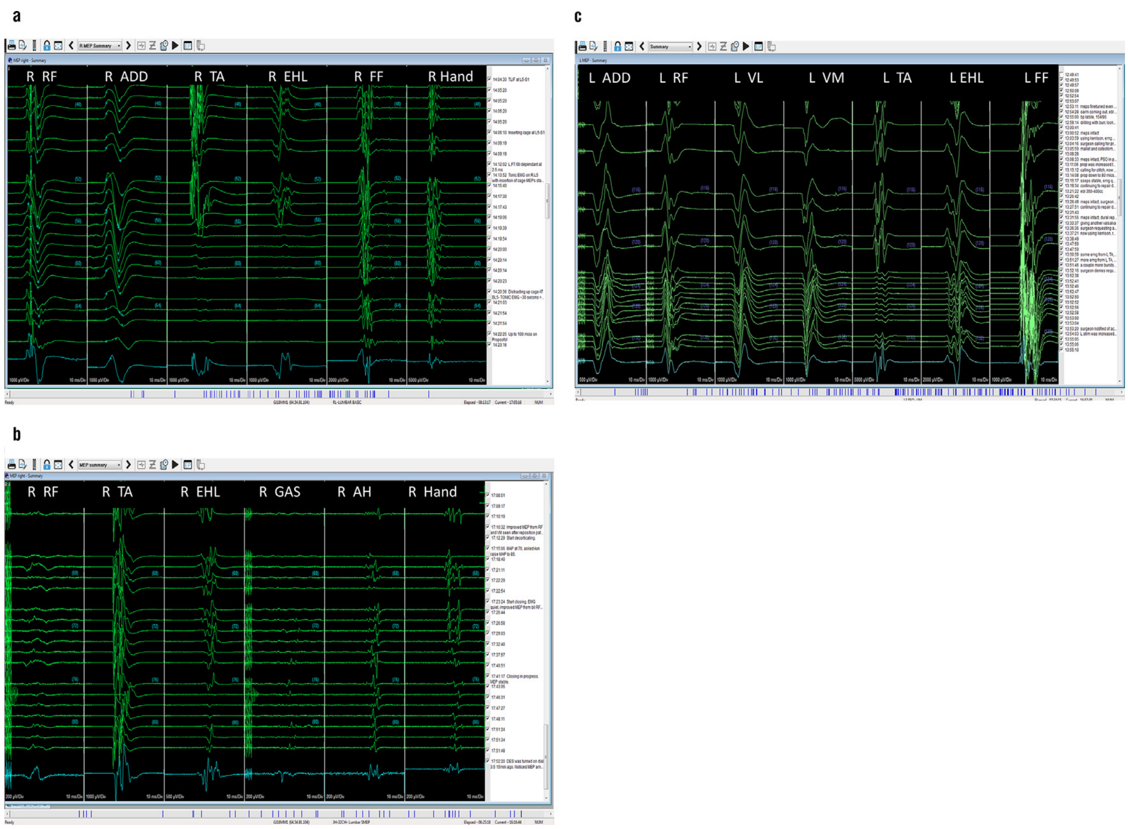

Fig. 1. Transcranial motor evoked potential (MEP) tracings obtained from 3 different patients who sustained intraoperative foot drop injuries during lumbar surgical repair. Individual MEP trials are in green; baseline values are shown at the bottom of the image in blue. Panel a shows significant decrease in MEP amplitude in both the Right TA and EHL myotomes during placement of interbody cage during grade 4 spondylolisthesis reduction. Tonic EMG was concurrent with MEP amplitude decrease. Panel b shows marked reduction in MEP amplitude of the Right EHL but minimal change in the R TA during closure of an L5 PSO. No tonic EMG activity was noted. Panel c depicts a large decrease in the Right TA amplitude but no changes in the EHL during closure of an L4 PSO. EMG activity was absent when MEP changes occurred.

R, right; L, left; RF, rectus femoris; ADD, adductor longus; TA, tibialis anterior; EHL, extensor hallucis longus; FF, foot flexors; GAS, gastrocnemius; AH, adductor hallucis; EMG, electromyography.

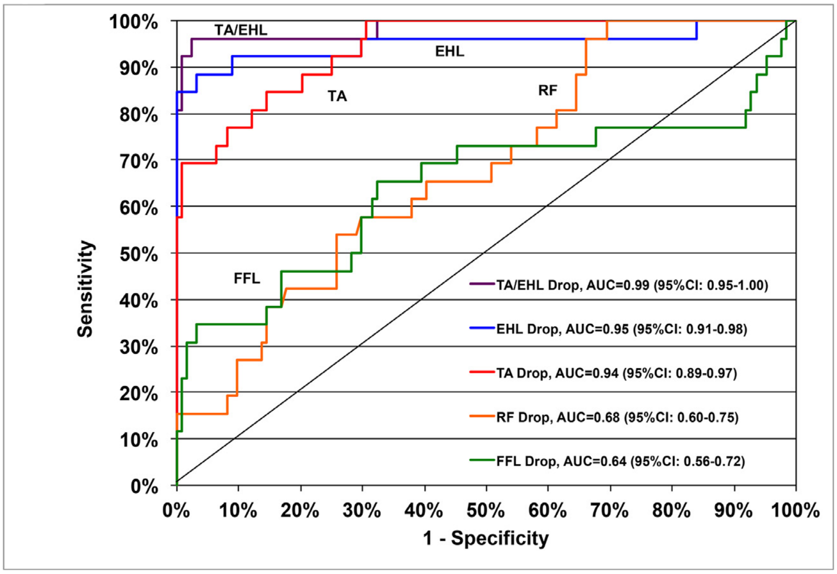

Fig. 2. Receiver operating characteristic curves of sensitivity vs 1-specificity for nerve injury/weakness of either the TA or EHL (TA/EHL). Individual curves are shown for the percent drop in transcranial motor evoked potential (MEP) amplitude of the monitored muscle groups. In addition to TA and EHL monitoring, foot flexors (FFL) and rectus femoris (RF) are shown for comparison. TA/EHL uses the maximum amplitude drop in either muscle. The area under the ROC curve (AUC) and 95% confidence intervals (CI) are shown for the various monitored muscles on the plot legend. The diagonal line indicates an AUC of 0.5.

detect a nerve root injury compared with previous reports [16−18,31−33]. Our study further challenges the fidelity of EMG monitoring for detecting a nerve root injury. Out of 25 injured patients, only 10 (40%) had an episode of tonic EMG that occurred concurrently with acute changes in the MEPs. Moreover, no patients had any significant EMG activity that suggested motor nerve injury without also having MEP amplitude changes.

Table 3
Net reclassification improvement for the addition of a motor group

Threshold	Added TP	Added FP	NRIe	NRIne	Total
Addition of EHL to monitoring TA for TA weakness					
20%	0	19	0.0%	−15.3%	−15.3%
30%	2	3	7.7%	−2.4%	5.3%
40%	3	1	11.5%	−0.8%	10.7%
50%	7	0	26.9%	0.0%	26.9%
60%	5	0	19.2%	0.0%	19.2%
70%	3	0	11.5%	0.0%	11.5%
80%	1	0	3.8%	0.0%	3.8%
90%	0	0	0.0%	0.0%	0.0%
Addition of TA to monitoring EHL for EHL weakness					
20%	0	21	0.0%	16.4%	−16.4%
30%	0	5	0.0%	3.9%	−3.9%
40%	0	2	0.0%	1.6%	−1.6%
50%	1	1	4.5%	0.8%	3.8%
60%	2	0	9.1%	0.0%	9.1%
70%	5	0	22.7%	0.0%	22.7%
80%	4	0	18.2%	0.0%	18.2%
90%	3	0	13.6%	0.0%	13.6%

TA, tibialis anterior; EHL, extensor hallucis longus; TP, True Positive; FP, false positive; NRIe, event net reclassification improvement; NRIne, nonevent reclassification improvement.

Threshold is the percent decrease in motor evoked potential.

NRIe = (Added TP − Added FN)/(TP + FN).

NRIne = (Added TN − Added FP)/(TN + FP).

Total = NRIe + NRIne.

MEP monitoring, in contrast, shows promise as a dependable predictor of dorsiflexion weakness. Yue et al. describes a case of an isolated foot drop injury that was accurately detected intraoperatively when the MEP response in the TA was lost [34]. Tamkus et al. reviewed 130 procedures involving instrumentation of L4−S1 [35]. They described five patients with new foot drop injury; three with severe deficits. They note significant decrease in the amplitude of the MEP responses of a single, combined TA-EHL myotome in those with serious weakness (<3/5).

Our study describes the pattern of TcMEP amplitude changes in the TA and/or EHL that occur with dorsiflexion injuries. Our results show that a persistent amplitude decrease in either myotome at the end of the surgical monitoring period strongly correlates with a new injury. The benefit of multimyotomal monitoring is highlighted by the examples provided in Fig. 1. MEP changes may be absent in either the TA or EHL, yet the patient may develop new foot drop weakness. Studies claiming failure of MEP monitoring to detect intraoperative nerve root injuries recorded responses from a single myotome [36−38]. This result should discourage monitoring of only a single muscle or “jumping” electrodes across multiple muscles [39]. Our data show that the accuracy of monitoring for a foot drop is enhanced if we monitor both the TA and the EHL.

Limitations

Our current results cannot be used to determine the optimal intraoperative MEP change that would elicit a warning alert to the surgeon. Many of our subjects sustained large

Table 4
Thresholds for the percent drop in motor evoked potential (MEP) amplitude with associated sensitivity, specificity, predictive values, and accuracy relative to the severity of dorsiflexion injury

Footdrop severity	MEP amplitude (% decrease)	PPV	NPV	Sens.	Spec.	Accuracy
	25%	41.3%	100.0%	100.0%	70.2%	92.0%
Any injury	30%	53.2%	99.0%	96.2%	82.3%	92.7%
(< 5/5)	40%	59.5%	99.1%	96.2%	86.3%	92.7%
	50%	86.2%	99.1%	96.2%	96.8%	92.7%
	60%	100.0%	95.4%	76.9%	100.0%	94.7%
	70%	100.0%	91.9%	57.7%	100.0%	96.7%
	80%	100.0%	87.3%	30.8%	100.0%	94.7%
	MEP amplitude (% Decrease)	PPV	NPV	Sens.	Spec.	Accuracy
	20%	34.6%	100.0%	100.0%	87.9%	88.7%
Severe injury	30%	36.0%	100.0%	100.0%	88.7%	89.3%
(< 3/5)	40%	36.0%	100.0%	100.0%	88.7%	89.3%
	50%	36.0%	100.0%	100.0%	88.7%	89.3%
	60%	45.0%	100.0%	100.0%	92.2%	92.7%
	70%	53.3%	99.3%	88.9%	95.0%	94.7%
	80%	62.5%	97.2%	55.6%	97.9%	95.3%

Threshold is the percent decrease in motor evoked potential.

TA, tibialis anterior; EHL, extensor hallucis longus; TP, True Positive; FP, false positive; NRIe, event net reclassification improvement; NRIne, nonevent reclassification improvement.

NRIe = (Added TP − Added FN)/(TP + FN).

NRIne = (Added TN − Added FP)/(TN + FP).

Total = NRIe + NRIne.

reductions in MEP amplitude (eg, >50%) during their surgical procedures. These MEP changes may have been due to surgical manipulation, increased anesthetic depth, or hemodynmic instability. These transient changes resolved and these subjects did not develop new weakness. We were not able to measure the frequency of these events nor correlate them to the patient's risk of developing an injury.

Our results suggest that relying on an 80% MEP amplitude decrease is too restrictive and may miss potential nerve root injuries [10]. We observed a mean MEP amplitude decrease of 65 ± 21% in the TA and 60 ± 26% in the EHL for patients experiencing weakness of one or more motor grades; more severe injuries (<3/5) were associated with an enduring loss of 75 ± 25% (TA) and 76 ± 17% (EHL). For detecting any injury, a 50% threshold may represents a desirable balance between sensitivity (96%) and specificity (97%). However, using a 50% threshold as an alarm criterion may produce a high rate of false positive alerts. A more restrictive alarm threshold, using a 60% decrease from baseline, would reduce false positives yet not miss any marked dorsiflexion weakness (<3/5), if the decline persists to the end of surgery.

We limited our study to include only patients with no dorsiflexion weakness before surgery. There may be very different changes to MEP responses from baseline when preexisting injury is present as compared with intact nerve roots.

Our analysis does not allow us to determine whether neuromonitoring can actually reduce the incidence of injury or improve long-term outcome. However, our findings of only nine serious injuries producing loss of antigravity function (1.6%) in a high-risk cohort, much lower than other published reports [4−11], suggest there may be a benefit − either lower incidence or lower severity of injury. In addition, although our database is incomplete, we observed most patients with 4/5 or 4+/5 weakness exhibited complete recovery of motor strength within 30−45 days after surgery. Of those nine with severe injury (<3/5), several demonstrated improvements of up to one motor grade by one year; others were lost to follow-up.

Finally, the technique used to obtain and maintain reliable MEP responses that allow for quantitative analysis is extremely difficult. Anesthesiologists must provide minimally suppressive anesthetic regimens and work hard to maintain hemodynamic homeostasis. Surgeons must allow neurophysiologists to perform frequent MEP trials, and also need to understand that many alerts may not reflect surgically produced injury. An appropriate response to intraoperative neuromonitoring changes, emphasizing communication between the neurophysiologist, anesthesiologist and surgeon, is critical. This can be facilitated by means of a checklist [40,41].

Summary

Intraoperative neurophysiological monitoring should be considered whenever the risk for nerve root injury that produces a foot drop is substantial. This should include reduction of high-grade spondylolisthesis and performance of a distal lumbar PSO. It remains controversial whether MEP monitoring is justified for less complex, lower risk spine procedures where the risk of nerve root injury is generally much smaller. Intraoperative MEP monitoring of both the TA and EHL muscles should be used to maximize sensitivity and specificity. Electromyography monitoring alone may miss a large number of injuries. However, EMG monitoring should be used as it is complementary to the use of MEPs, and often serves to trigger a prompt MEP trial. Additional prospective studies are warranted to determine whether MEP monitoring may prove to be as accurate for other spinal nerve roots.

References

[1] Schirmer CM, Shils JL, Arle JE, et al. Heuristic map of myotomal innervation in humans using direct intraoperative nerve root stimulation. J Neurosurg: Spine 2011;15:64–70.

[2] Young A, Getty J, Jackson A, et al. Variations in the pattern of muscle innervation by the L5 and S1 nerve roots. Spine 1983;8:616–24.

[3] Pateder D, Kostuik J. Lumbar nerve root palsy after adult spinal deformity surgery. Spine 2005;30(14):1632–6.

[4] DeWald C, Vartabedian J, Rodts M, et al. Evaluation and management of high-grade spondylolisthesis in adults. Spine 2005;30: S49–59.

[5] Maurice H, Morley T. Cauda equina lesions following fusion in situ and decompressive laminectomy for severe spondylolisthesis. Four case reports. Spine 1989;14:214–6.

[6] Hu S, Bradford D, Transfeldt E, et al. Reduction of high-grade spondylolisthesis using Edwards instrumentation. Spine 1996;21:367–71.

[7] Sailhan F, Gollogly S, Roussouly P. The radiographic results and neurologic complications of instrumented reduction and fusion of high-grade spondylolisthesis without decompression of the neural elements: a retrospective review of 44 patients. Spine 2006;31:161–70.

[8] Kasliwal M, Smith J, Shaffrey C, et al. Surgery for high-grade spondylolisthesis in adults and pediatric patients: a report from the scoliosis research society morbidity and mortality database. Neurosurgery 2012;71:109–16.

[9] de Kunder S, van Kuijk S, Kim Rijkers K, et al. Transforaminal lumbar interbody fusion (TLIF) versus posterior lumbar interbody fusion (PLIF) in lumbar spondylolisthesis: a systematic review and meta-analysis. Spine J 2017;17:1712−1721.

[10] Lieberman J, Lyon R, Feiner J, et al. The efficacy of motor evoked potentials in fixed sagittal imbalance deformity correction surgery. Spine 2008;33:E414–24.

[11] Buchowski J, Bridwell K, Lenke L, et al. Neurologic complications of lumbar pedicle subtraction osteotomy: a 10-year assessment. Spine 2007;32:2245–52.

[12] Lenke L, Fehlings M, Shaffrey C, et al. Neurologic outcomes of complex adult spinal deformity surgery: results of the prospective, multicenter Scoli-RISK-1 study. Spine 2016;41:204–12.

[13] Beatty R, McGuire P, Moroney J, et al. Continuous intraoperative electromyographic recording during spinal surgery. J Neurosurg 1995;82:401–5.

[14] Owen J, Kostuik J, Gornet M, et al. The use of mechanically elicited electromyograms to protect nerve roots during surgery for spinal degeneration. Spine 1994;19:1704–10.

[15] Nichols G, Manafov E. Utility of electromyography for nerve root monitoring during spinal surgery. J Clin Neurophysiol 2012;29: 140–8.

[16] Bhalodia V, Schwartz D, Sestokas A, et al. Efficacy of intraoperative monitoring of transcranial electrical stimulation-induced motor evoked potentials and spontaneous electromyography activity to identify acute-versus delayed-onset C-5 nerve root palsy during cervical spine surgery. Journal of Neurosurgery: Spine 2013;19:395–402.

[17] MS Valone F, Lyon R, Lieberman J, et al. Efficacy of transcranial motor evoked potentials, mechanically elicited electromyography, and evoked electromyography to assess nerve root function during sustained compression in a porcine model. Spine 2014;39:E989–93.

[18] Lyon R, Lieberman J, Feiner J, et al. Relative efficacy of transcranial motor evoked potentials, mechanically-elicited electromyography, and evoked EMG to assess nerve root function during sustained retraction in a porcine model. Spine 2009;34:E558–64.

[19] Jou I. The effects from lumbar nerve root transection in rats on spinal somatosensory and motor-evoked potentials. Spine 2004;29:147–55.

[20] Resnick D, Choudhri T, Dailey A, et al. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 15: electrophysiological monitoring and lumbar fusion. J Neurosurg Spine 2005;2:725–32.

[21] Tsai S, Tsai C, Wu P, et al. Intraoperative use of somatosensory-evoked potential in monitoring nerve roots. J Clin Neurophysiol 2012;29:110–7.

[22] Toleikis J. Intraoperative monitoring using somatosensory evoked potentials. A position statement by the American Society of Neurophysiological Monitoring. J Clin Monit Comput 2005;19:241–58.

[23] Mok J, Lyon R, Lieberman JA, et al. Monitoring of nerve root injury using transcranial motor-evoked potentials in a pig model. Spine 2008;33:E465–73.

[24] Macdonald D, Stigsby B, Al Homoud I, et al. Utility of motor evoked potentials for intraoperative nerve root monitoring. J Clin Neurophysiol 2012;29:118–25.

[25] Sutter M, Eggspuehler A, Grob D, et al. Multimodal intraoperative monitoring (MIOM) during 409 lumbosacral surgical procedures in 409 patients. Eur Spine J 2007;16:S221–8.

[26] Langeloo D, Lelivelt A, Louis Journée L, et al. Transcranial electrical motor-evoked potential monitoring during surgery for spinal deformity: a study of 145 patients. Spine 2003;28:1043–50.

[27] Lyon R, Feiner J, Lieberman J. Progressive suppression of motor evoked potentials during general anesthesia: "The Phenomenon of ‘‘Anesthetic Fade.’’. J Neurosurg Anesthesiol 2005;17:13–9.

[28] Bose B, Wierzbowski L, Sestokas A. Neurophysiologic monitoring of spinal nerve root function during instrumented posterior lumbar spine surgery. Spine 2002;27:1444–50.

[29] Leening M, Vedder M, Witteman J, et al. Net reclassification improvement: computation, interpretation, and controversies: a literature review and clinician’s guide. Ann Intern Med 2014;160:122–31.

[30] Meyerding H. Spondylolisthesis. Surg Gynecol Obstet 1932;54:371–7.

[31] Gunnarsson T, Krassioukov A, Sarjeant R, et al. Real-time continuous intraoperative electromyographic and somatosensory evoked potential recordings in spinal surgery: correlation of clinical and electrophysiologic findings in a prospective, consecutive series of 213 cases. Spine 2004;29:677–84.

[32] Quraishi N, Lewis S, Kelleher M, et al. Intraoperative multimodality monitoring in adult spinal deformity: analysis of a prospective series of one hundred two cases with independent evaluation. Spine 2009;34:1504–12.

[33] Bose B, Sestokas A, Schwartz D. Neurophysiological detection of iatrogenic C-5 nerve deficit during anterior cervical spinal surgery. J Neurosurg Spine 2007;6:381–5.

[34] Yue Q, Hale T, Knecht A, et al. Intraoperative loss of tibialis anterior transcranial electrical motor evoked potentials predicted postoperative foot drop. World Neurosurg 2017;755:e1–755.e3.

[35] Tamkus A, Rice K, Hoffman G. Transcranial motor evoked potential alarm criteria to predict foot drop injury during lumbosacral surgery. Spine 2018; 43:E227−33.

[36] Schär R, Sutter M, Mannion A, et al. Outcome of L5 radiculopathy after reduction and instrumented transforaminal lumbar interbody fusion of high-grade L5−S1 isthmic spondylolisthesis and the role of intraoperative monitoring. Eur Spine J 2017;26:679–90.

[37] Chen Y, Wang B, Yang J, et al. Neurophysiological monitoring of lumbar spinal nerve roots: A case report of postoperative deficit and literature review. Int J Surg Case Rep 2017;30:218–21.

[38] Ohashi M, Watanabe K, Furutani K, et al. False-negative transcranial motor evoked potentials (TcMEPs) during surgery for congenital

lumbar kyphoscoliosis: a case report. Spinal Cord Ser Cases 2017;3:17053.

[39] Lyon R, Burch S, Lieberman J. Mixed-muscle electrode placement ("jumping" muscles) may produce false-negative results when using transcranial motor evoked potentials to detect an isolated nerve root injury in a porcine model. J Clin Monit Comput 2009;23:403–8.

[40] Vitale M, Skaggs D, Pace G, et al. Best practices in intraoperative neuromonitoring in spine deformity surgery: development of an intraoperative checklist to optimize response. Spine Deform 2014;2:333–9.

[41] Ziewacz J, Berven S, Mummaneni V, et al. The design, development, and implementation of a checklist for intraoperative neuromonitoring changes. Neurosurg Focus 2012;33:E11.