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Original Investigation

Multimodal Intraoperative Neurophysiological Monitoring in Neurosurgical Oncology

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ABSTRACT

AIM: Neurosurgical oncology that is performed for lesions located in critical areas like the sensorimotor area has additional risk because it may cause serious neurological deficiencies. Some intraoperative neuromonitoring (IONM) modalities can effectively help the surgeons to maximize resections of this kind of lesions with or without an acceptable neurological deficiency. Our aim was to share our IONM experiences with patients who underwent intracranial lesion surgery in critical areas between September 2013 and January 2015.

MATERIAL and METHODS: This retrospective study was performed on 31 patients who underwent brain surgery for the resection of lesions located in eloquent areas. Demographic characteristics, lesion localizations, lesion pathologies, surgery, IONM recordings, and pre- and postoperative neurological examinations were reviewed.

RESULTS: Five of the 31 patients had lesions in the cerebellopontine angle and 26 patients had lesions close to critical locations. Transcranial motor evoked potentials and somatosensory evoked potentials were performed in 27, electroencephalography in 31, auditory evoked potentials in 8, visual evoked potentials in 2, triggered electromyography in 8, and central sulcus determination and brain mapping in 17 patients. Motor evoked potential changes occurred in 2 patients intraoperatively. One had right hemiparesia lasting 3 days while the other had monoparesia which improved within 2 months. Permanent neurological deficit was not observed.

CONCLUSION: Intraoperative neuromonitoring helps the surgeons to maximize resection of lesions in or close to eloquent areas of the brain. Using only one modality is not sufficient, whereas a combination of modalities is required to obtain a better outcome.

KEYWORDS: Neurosurgical oncology, Evoked potentials, Multimodality, Intraoperative monitoring

INTRODUCTION

Neurosurgical oncology procedures performed for lesions placed in or close to the eloquent cortical areas carry increased risk of neurological deficits, such as dysarthria, aphonia, paralysis and paresthesia. Therefore, neurophysiological monitoring is essential for almost all operations in or around critical locations of the brain.

Intraoperative neurophysiological monitoring (IONM) is the use of electrophysiological methods to define the critical neural structures and to monitor their functional integrity during the surgery. The electrophysiological methods used in the brain are evoked potentials (Somatosensory Evoked Potentials-SSEP, Motor Evoked Potentials-MEP, visual evoked potential-VEP, auditory evoked potential-AEP), electrocorticography (ECoG) and electromyography (EMG). It is usually necessary to combine neurophysiological tests; this kind of combination is called “multimodality” as the testing covers different neural structures under risk in the brain surgery.

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Both direct cortical stimulation (DCS) and transcranially triggered MEPs (tcMEPs) are used in monitoring of the corticospinal tract in supratentorial surgery, whereas tcMEPs are mainly used for monitoring the spinal cord. SSEP recording is useful for defining central sulci and assessing the integrity of the large fibers of the somatosensory system during brain surgery.

With regards to cranial nerve (CN) monitoring, free-running EMG (fEMG) and triggered EMG (tEMG) are essential. Free-running EMG records spontaneous muscle activity, thus allowing real-time assessment. This technique can detect surgically driven mechanical irritation of CNs during cranial surgery and of peripheral nerves during spinal surgery. This provides a warning to the surgeon before an irreversible damage occurs. In the tEMG technique, an electrical stimulus is applied directly on the cranial and peripheral nerves to determine their location and control the functions of injured nerve by assessing transmission of the electrical stimulation through the structures and also to compare them with the healthy baselines (18). Intraoperative ECoG is used for mapping of seizure foci and monitoring for afterdischarges in functional mapping in cranial surgery (9,16,19).

In this study, we evaluated our IONM findings from 31 patients who underwent intracranial surgery for lesions located in, or in close proximity to critical neural structures between September 2013 and January 2015.

MATERIAL and METHODS

Patient Population

Multimodal IONM was performed during surgery in 31 cases, including 5 cerebellopontine angle (CPA) lesion surgeries and 26 other intracranial surgeries close to the pyramidal tract or other critical locations between September 2013 and January 2015 (Table I). These patients consisted of 18 males (60%) and 13 females. The mean age of the patients was 45 years (age range 8–70 years).

Monitoring

Monitoring was performed using the Medtronic NIM-Eclipse system version 3.5.353 for IONM by a single technician and 2 clinical neurophysiologists (E.T, S.B). MEPs were recorded to assess the motor pathways while SSEPs were used to monitor the sensory pathways in the dorsal columns and to define central sulcus localization. In addition, direct CN stimulation, fEMG, AEP and, ECoG were performed as required. All surgical procedures were followed on the visual screen in the operating room during surgery.

Recording muscles were determined according to the lesion's location and surgical approach. The stainless still needle electrodes (13 mm, Medtronic) were used to record muscle responses for MEPs and EMG as well as stimulating peripheral nerves for SSEP. Disposable corkscrew (CS) electrodes were used for stimulation of tcMEPs and also for recording of cortical SSEPs. Subdural recording electrodes with 6 or 8 contact were used for determining central sulcus location via median SSEP recording and phase reversal technique.

Fifth, seventh and eighth CNs were all monitored for surgery in CPA, petroclival region and also brainstem. Electrodes were placed bilaterally in the orbicularis oris (OOR) muscle, with contralateral OOR being control, lesion sided orbicularis oculi and mentalis muscles innervated 5th and 7th CNs (14).

The stimulating electrodes for tcMEPs were placed at C1/C2 for the lower extremity responses and C3/C4 for responses from the upper extremities and facial muscles (according to the international 10-20 system for EEG). TcMEP responses were recorded from the appropriate muscles contralateral to the lesion location. Double train stimulation was used for tcMEP. Each train consisted of 5 pulses of 0.5 ms duration with an interstimulus interval (ISI) of 3 ms. Stimulation intensities varied between 200-400 V according to the individual. Stimulus duration was 50 ms.

Upper extremities' SSEPs were obtained by stimulating median or ulnar nerves and recording cortically with an electrode montage of C3'-FPz/C4'-FPz, while the lower extremities' SSEPs were obtained by stimulating the tibial nerves recording from cortical Cz'-FPz. All stimulations were performed bilaterally with interleaving stimulation for upper and lower extremities.

SSEP recordings were set up with a sensitivity of 0.5 μV/mm and a sweep speed of 100 msec; filter settings were set to 100-300 Hz; the stimulus frequency was 1.7 Hz, and the stimulation duration was 500 μs for tibial nerve and 300 μs for the median/ulnar nerve. The mean stimulus intensity was 20 and 30 mA for median/ulnar and tibial nerves, respectively.

Monitoring was started immediately after anesthesia induction and continued until the termination of the surgical procedure, as recommended by the American Clinical Neurophysiology Society in 2009 (17).

Anesthesia

Total intravenous anesthesia (TIVA) using propofol and analgesic drugs (remifentanil or fentanyl) was used in all cases. We avoided using the volatile anesthetics because they reduce the tcMEP amplitude significantly more than propofol (2,12,20,21). A short half-life muscle relaxant was used only during the tracheal intubation procedure. The elimination of the muscle relaxant was confirmed by performing train of four (TOF). A bite block was placed to prevent tongue injuries during intraoperative TcMEP monitoring.

RESULTS

Thirty-one patients were included in this study with an age ranging from 8 to 70 years (with a mean age of 45 years). There were 18 males and 13 females. For 20 patients, gross total tumor removal was performed during the surgery where subtotal tumor removal was performed in 10 patients. Tumors' localizations and sizes, extent of resections, tumors' pathologies, pre- and postoperative neurological examinations and IONM changes in this series are summarized in Table I. The most common surgery was related to lesions located in or around the motor cortical area (29%).

Table I: Tumor Localization, Extent of Resection, Tumor Pathology, Pre- Postoperative Neurological Examination, Intraoperative IONM findings

Case No	Tumor Localization	Lesion Size	Pathology	Extent of Resection	Preoperative Neurological Examination	Postoperative New Neurological Deficit	Intraoperative IONM Findings
1	L CPA	3.5x3.5x2 cm	schwannoma, WHO grade 1	GT	L deafness	L facial paresis HB1	fEMG spontaneous activity tEMG: no change
2	L Petroclival region	6x6x7 cm	meningioma	ST	diplopia, facial paresis	absent	stable
3	L CPA	4x4x3 cm	schwannoma	GT	L deafness	L facial paresis HB2	fEMG spontaneous activity tEMG: no change
4	L CPA	12x20x18 mm	meningioma	GT	normal	absent	stable
5	L CPA	5.5x5.x5 cm	schwannoma, grade 1	GT	L facial mild paresis, atrophy in L trapezius and sternocleidomastoid muscles	absent	stable
6	Medulla Oblongata	-	pilocytic astrocytoma	ST	tetraparesis, absent gag reflex	absent	MEP loss Final MEP: partial improvement
7	L CPA	3x3x4 cm	meningioma	ST	Normal	absent	stable
8	L Precentral Gyrus	3x2x3 cm	oligodendroglioma	ST	normal	absent	stable
9	L Precentral Gyrus	4x4x3 cm	metastasis (colon)	GT	normal	absent	stable
10	L Precentral Gyrus	3x3x4 cm	diffuse astrocytoma	GT	normal	R hemiparesis	stable*
11	L Supplementary Motor Area	3x2x3 cm	GBM	GT	R hemiparesis	absent	stable
12	R Parietotemporal	3x3x4 cm	GBM	GT	L hemiparesis	absent	stable
13	L Frontotemporal Deep Localized	3x3x4 cm	anaplastic oligoastrocytoma	GT	normal	absent	stable
14	R Parietal (central sulcus)	4x4x5 cm	meningioma, grade 2	GT	normal	absent	stable
15	L Frontocentral	4x4x3 cm	GBM	GT	R hemiparesis, aphasia	absent	stable
16	L Frontotemporal	6.5x4x4.5	anaplastic oligoastrocytoma	ST	R facial mild paresis	absent	stable
17	L Frontoparietal	4x5x4.5 cm	germ cell tm	GT	R hemiparesis	absent	stable
18	L Frontocentral	3x2x3 cm	diffuse astrocytoma	GT	normal	absent	stable
19	R Temporoparietal	3x3x3 cm	GBM	GT	normal	absent	stable
20	Corpus Callosum	4x5x4 cm	high grade glioma	biopsy	R hemiparesis	absent	stable

Table I: Cont.

Case No	Tumor Localization	Lesion Size	Pathology	Extent of Resection	Preoperative Neurological Examination	Postoperative New Neurological Deficit	Intraoperative IONM Findings
21	Bifrontal Parafalcine	7x7x6 cm	meningioma (grade 2)	GT	normal	absent	stable
22	L Frontal Parasagittal	3x4x4 cm	astrocytoma grade 1	GT	normal	R foot drop	MEP loss
23	L Intrahemispheric Deep Localized	5x5x4 cm	high grade glioma	ST	absent	R hemiparesis, dysphagia	fEMG: spontaneous activity on muscles innervated 5th and 7th cranial nerves MEP: stable
24	Mesencephalon	3x3x2 cm	anaplastic ependymoma	ST	diplopia, ataxia	absent	fEMG: spontaneous activity on muscles innervated 5th and 7th cranial nerves MEP: stable
25	R Cingulate Cortex and Corpus Callosum	18x17 mm	diffuse astrocytoma	GT	normal	absent	stable
26	L Insular	2x2x2 cm	diffuse astrocytoma	ST	normal	absent	stable
27	R Temporoparietal	4x4x3 cm	high grade glioma	GT	L hemiparesis	absent	stable
28	R Temporooccipital	4x4x3 cm	metastasis (lung)	GT	normal	absent	stable
29	Sphenoid Wing	7x7x6 cm	meningioma	ST	normal	absent	stable
30	Tuberculum Sella	2x2x3 cm	meningioma	ST	L Temporal hemianopsia	absent	stable
31	L Precentral Gyrus	3x4x3 cm	diffuse astrocytoma	GT	normal	absent	stable

CPA: *Cerebellopontine angle,* ***GBM:*** *Glioblastoma,* ***WHO:*** *World Health Organization,* ***R:*** *Right,* ***L:*** *Left,* ***GT:*** *Gross total (91-100%),* ***ST:*** *Subtotal (51-90%), biopsy (1-10%),* ***HB:*** *House-Brackmann-Grading,* ***Stable:*** *No MEP changes or decrement <50%,* ***IONM:*** *Intraoperative Neuromonitoring,* ***fEMG:*** *Free-running electromyography,* ***MEP:*** *Motor evoked potentials,* ***EEG:*** *Electroencephalography,* ***tcMEP:*** *transcranial stimulation for motor evoked potentials.*

** Only central sulcus determination, brain mapping and EEG were performed in this patient. tcMEP were not performed during the surgery.*

We performed MEP, SSEPs and free-running EMG in all patients. In addition, direct cortical stimulation was performed in 17 patients and nerve stimulation triggered EMG was applied in seven patients by the same neurosurgeon. A monopolar and/or bipolar probe was used to stimulate and to objectively identify the facial nerve branches in the surgical field and also check the function of any injured facial nerves by assessing the electrical transmission through such structures and comparing it with a healthy baseline. We stimulated in small increments of 0.1 mA, starting at 0.1 mA and increasing up to 1 mA with repetitive square wave pulses of 0.1-0.2 msec, at a frequency of 4 Hz averaging 4-8 trials.

All significant changes in CN nuclei monitoring included in fEMG and tEMG were immediately relayed to the operating surgeon. In cases where neurotonic activity was felt to be due to excessive traction or manipulation of the brainstem, surgery was paused and continued only if the neurotonic activity diminished or disappeared with less manipulation.

Transcranial motor evoked potentials were evaluated in 34 patients (biphasic stimulation, 5 train/300 Hz, ISI 3 ms, 200-400 V). The most common monitored muscles for tcMEP were the abductor pollicis brevis (APB), extensor digitorum communis, abductor hallucis, and anterior tibialis muscles on the contralateral side and also ipsilateral APB was used as control to rule out systemic effects and differentiate changes due to surgery in or around the pyramidal tracts.

Other modalities used included EEG in 30 patients, SSEPs (3 Hz, 10-30 mA) in 34 patients, AEP (100dB, 1000 average, 20 Hz) in nine patients, VEP (Google, duration 10 ms, luminescence 500 Lx, rate 0.9 Hz) in two patients, and triggered EMG (0.05-5mA) in nine patients. Cranial mapping with a monopolar stimulator (200 μs, 1-8 mA stimulation, 5 train/500 Hz) was performed in 7 patients. Central sulcus determination was performed using phase reversal technique with upper median SSEPs in 17 patients. Steady recordings were not obtained in five patients because of technical problems, anatomical displacement or edema related tumor.

MEP changes were observed in two patients (Cases 6 and 22, Table I) as defined by a decrease in responses of more than 50% or MEP loss according to baseline. MEP loss of Case 6 improved partially at the end of surgery and did not have any new neurological deterioration postoperatively. Case 22 had foot drop that recovered after 2 months. Neurological deterioration was presented in five patients (Table I). Facial paresis was presented in 2, hemiparesis in 1, hemiparesis and dysphagia in 1 patient. Case 10 had hemiparesis that recovered in a few hours where hemiparesis and dysphasia in Case 23 lasted 3 days. Case 23 had not change in MEP during the surgery.

Case illustration (No.22 in Table I)

A 22-year-old man presented with headache. Preoperative magnetic resonance imaging (MRI) showed left parasagittal mass lesion located in frontal region (Figure 1A, B). Loss of MEP developed during the resection and was ended up the surgery (Figure 1C, D). This patient presented with foot drop postoperatively. The tumor was removed gross totally (Figure 1E, F). Final pathology consisted of grade 1 astrocytoma.

■ DISCUSSION

Supratentorial tumors may require functional cortical mapping with several tests, such as phase reversal of median nerve SSEPs, DCS triggered by direct electrical cortical stimulation, and ECoG for revealing the baseline cortical activity and afterdischarges, which carry a seizure risk and can also result from repeated electrical stimulations. In the present study, it was demonstrated that multimodal IONM is important in the brain surgery to successfully remove lesions located in or near the critical areas.

We observed a tcMEP change in two patients, but neurological deficit in five (Table I). This may be related to only transcranial cortical stimulation use without directly stimulating the cortex in the supratentorial regions and also facial EMG as a single modality for protecting cranial nerves, especially for the facial nerve, in posterior fossa lesions. There are some reports that parallel use of DCS and tcMEPs improves the sensitivity of intraoperative detection of motor impairment. DCS may be superior to tcMEP during brain tumor resection (10).

We used a monopolar and/or bipolar probe to stimulate and objectively identify facial nerve branches based on the lesion location and the relationship between the facial nerve and lesion in the cerebellopontine angle tumor surgeries. It is known that using bipolar stimulation requires less current for stimulation and also reduces the current spread. However, current shunting may occur in the case of increased amount of fluid, especially when the stimulating prongs are too close each other. On the contrary, monopolar stimulation is prone to current spread in the surgical field and because of this, tends to be more sensitive and less specific at depolarizing and detecting nerves. We stimulated the facial nerve in small increments of 0.1 mA, starting 0.1 mA going up to 1 mA with repetitive square wave pulses of 0.1-0.2 msec, with a frequency 4 Hz, averaging 4-8 trials. We started stimulation with 0.1 mA because Kimura found that stimulation at less than 0.05 msec was ineffective and also the stimulation with a pulse of >1 msec in width was not tolerable (7). We also never increased the intensity by more than 1 mA (at the 0.2 msec pulse duration) because of the risk of injury to directly stimulated tissue. Injury effect, however, is not only related to stimulus intensity, but also pulse duration, pulse frequency, and electrode surface area. Chang et al. described a technique of stimulating CNs nuclei where he started the stimulation at 0.1 mA, with increments of 0.1 mA and continued until 10-12 mA (1).

We used both fEMG and tEMG in all CPA tumor surgeries. In alignment with a previous report (15), we found a stimulus threshold of 0.05 mA or less was a useful criterion to assess facial nerve function postoperatively. If using voltage, a response amplitude of 240 μV or greater is another predictor of postoperative facial nerve function (13). Though the use of facial nerve threshold and amplitude together is superior to threshold alone as a predictor of postoperative facial nerve function, we could not evaluate response amplitudes and stimulus threshold together in terms of saved facial nerve functions because of artifacts (13,15).

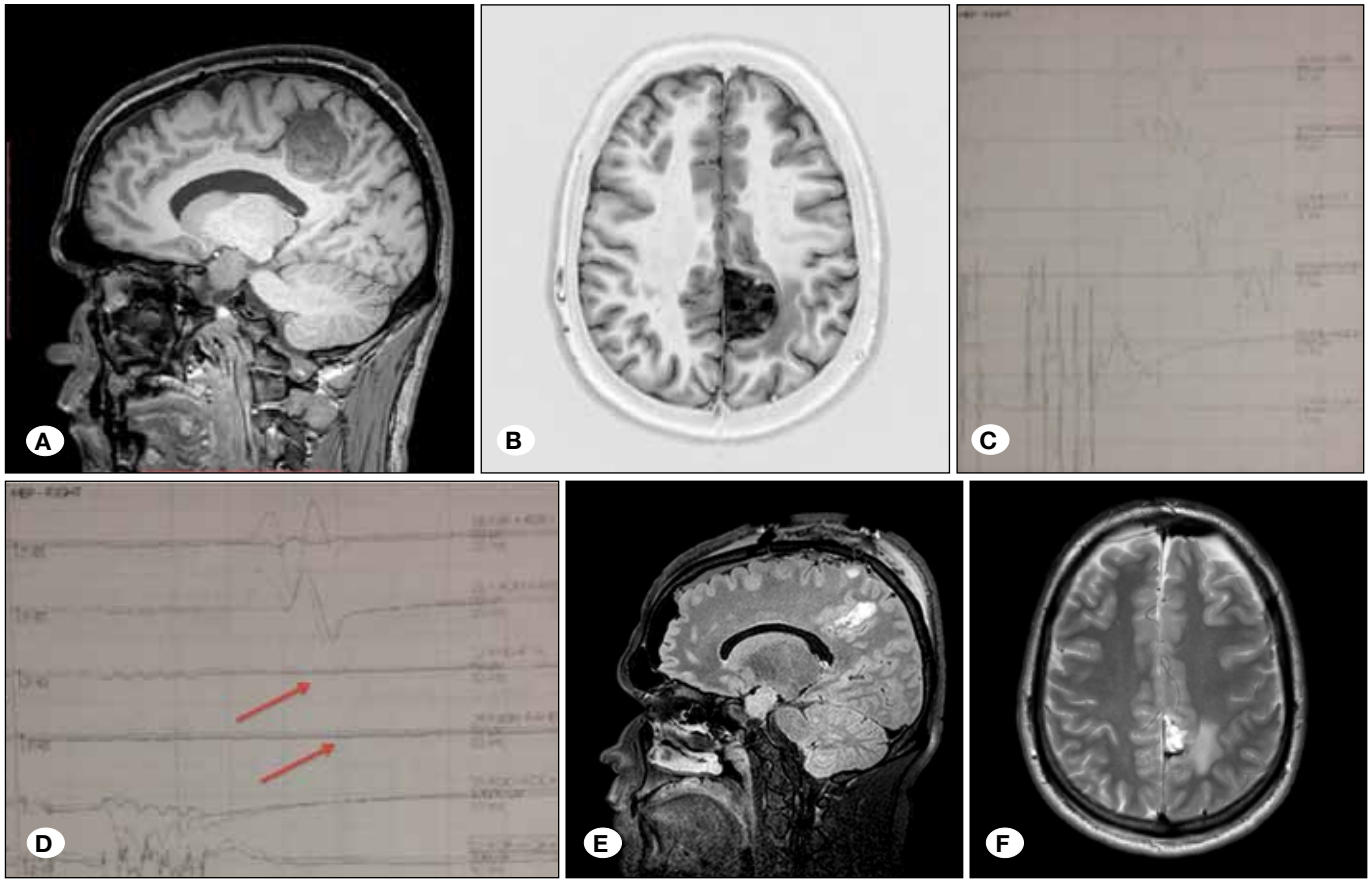

Figure 1: A, B) Enhanced T1-weighted sagittal and axial MRI showing a 3x4x4 cm-sized parasagittal mass lesion in the left frontal lobe. **C, D)** MEP responses lost in the left lower extremity at the end of the resection. **E, F)** Postoperative sagittal and axial MRI of the patient.

We did not observe SSEP changes. Central sulcus determination was performed using the phase reversal technique with upper median SEP which is one of the most commonly used methods for defining the central sulcus (8). Steady recordings could not be obtained in three of these patients because of technical problems, anatomical displacement or edema related to the tumor.

The posterior fossa has many vital structures such as CNs brainstem structures, cerebellum and spinal cord, all located in close proximity to each other. Identifying these structures can be difficult in cases of large tumors and displaced anatomical structures. It has been shown that the sensitivity and specificity are high for multimodal IONM with SSEPs and MEPs as compared to using only one modality (4). Feng et al. retrospectively reviewed 176 patients who underwent spinal surgery and were monitored with either tcMEPs or SSEPs or tcMEPs together with SSEPs. Just using SSEPs had specificity (92%) but no sensitivity. Therefore it could detect only about half the cases of nerve injury. MEP monitoring by itself had high sensitivity (92%) and specificity (95%). Combining SSEP and MEP monitoring revealed the highest performance in term of both sensitivity (93%) and specificity (99%)(4). Using MEP and SSEP together is better for identification and monitorization during posterior fossa surgeries.

Motor evoked potentials induced by direct electrical cortical stimulation are preferred over tcMEP, as they create more discrete areas of stimulation and avoid deep stimulation of the descending motor pathways, distal to the level of the intracranial surgery. Lack of DCS is the major weakness of this study. This modality could not be added to our set up because of our limited experience. In order to remove this deficiency, however, some other advanced techniques such as intraoperative MRI, preoperative diffusion tensor imaging (DTI) and/or intraoperative ultrasound were used in the selected cases in addition to intraoperative monitoring. In addition, lack of corticobulbar MEP for monitoring of facial nerve in the CPA, petroclival region and brainstem areas is the other weakness. In the literature, corticobulbar MEP recorded by C3/C4-Cz montage reliably produced facial MEPs in 50 patients and using 50% of baseline amplitude criteria, significant facial deficits were predicted with a sensitivity/specificity of 1.00/0.88 (3). Facial MEPs were also declared as highly reliable in predicting early and late postoperative function (14).

The other weakness was related to the lack of D wave recording. D wave is recorded directly from spinal cord is an essential complementary method to monitor the spinal cord and is considered as the “gold standard” to monitor corticospinal tract

functional integrity. They are non-synaptic, linear, stable, and resistant to anesthesia and neuromuscular blockade. Generally, D waves are used to monitor the corticospinal tract during certain spinal cord surgeries. While Katayama investigated the use of D waves by recording from electrodes inserted into the spinal epidural space to monitor the corticospinal tract during supratentorial tumor removal (6), afterwards it was reported that muscular MEP was a more sensitive method than D wave for detecting immediate motor cortical damage (5). More recently, new guidelines have stipulated that the D-wave warning criteria is an amplitude reduction with no other confounding explanation: >50% for intramedullary spinal cord tumor surgery, and >30-40% for peri-rolandic surgery (11). Since D-wave recording has only recently been recommended as an additional helper modality in supratentorial surgeries, this was not actually a weakness in this study. Therefore, the use of D waves in the future may be added to MEPs because it is a predictor of clinical outcome postoperatively.

CONCLUSION

Intraoperative neuromonitoring is a developing practice in our country, performed at international standards at a limited number of centers. Thus, published cases and reports about IONM are limited. We aimed to contribute to the literature and also share our experiences, reviewing our cranial cases as a newly established neuromonitoring unit.

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