



Intraoperative Neurophysiologic Examination in Central Nervous System Tumor Surgery: Four-year Single-institution Experience

Merkezi Sinir Sistemi Kitle Cerrahisi Ameliyatlarında İntraoperatif Nörofizyolojik İnceleme: Dört Yıllık Tek Hastane Tecrübesi

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Abstract

Objective: Intraoperative neurophysiologic monitoring (IONM) is widely used nowadays to minimize neurologic morbidity in neurosurgical operations. Our goal was to describe the standard IONM techniques used in our center and to discuss our own clinical experience with a multimodality approach.

Materials and Methods: All consecutive adult patients consulted for neurosurgical operations who underwent at least one modality of IONM (brainstem-evoked potential, motor-evoked potential, somatosensory-evoked potential, and/or electromyography) were retrospectively reviewed.

Results: Twenty-eight patients who underwent central nervous system tumor surgery between 2012 and 2016 received IONM. IONM minimizes the neurologic morbidity of surgery and allows identification and differentiation of functional neural tissues.

Conclusion: Multimodal IONM is a valuable tool for optimization of outcomes in complex central nervous system surgery.

Keywords: Central nervous system tumor surgery, intraoperative monitoring, somatosensory-evoked potential, brainstem-evoked potential, motor-evoked potential

Öz

Amaç: İntraoperatif nörofizyolojik monitörizasyon (İONM), beyin cerrahisi operasyonlarında nörolojik kaybı en aza indirmek için günümüzde oldukça yaygın şekilde kullanılmaktadır. Amacımız, merkezimizde kullanılan standart İONM tekniklerini tanımlamak ve çoklu modalite yaklaşımına sahip kendi klinik tecrübemizi tartışmaktır.

Gereç ve Yöntem: Tüm beyin cerrahisi operasyonları için danışılan ve en az bir modaliteli İONM (beyin sapı uyarılmış potansiyel, motor uyarılmış potansiyel, somatosensoryel uyarılmış potansiyel ve/veya elektromiyografi) yapılan erişkin hastalar geriye dönük olarak gözden geçirildi.

Bulgular: 2012-2016 yılları arasında merkezi sinir sistemi kitle cerrahisi olan 28 hastaya İONM uygulandı. İONM cerrahinin nörolojik morbiditesini en aza indirmektedir ve fonksiyonel nöral dokuların tanınması ve ayrımını sağlamaktadır.

Sonuç: Çoklu modaliteli İONM karmaşık merkezi sinir sistemi cerrahisinde sonucun en iyi şekilde olmasını sağlayan değerli bir araçtır.

Anahtar Kelimeler: Merkezi sinir sistemi kitle cerrahisi, intraoperatif nörofizyolojik izleme, somatosensoryel uyarılmış potansiyel, beyin sapı uyarılmış potansiyel, motor uyarılmış potansiyel

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Introduction

Intraoperative neurophysiologic monitoring (IONM) is used to minimize morbidity in tumor surgeries. Due to its anatomic sensitivity, intraoperative use of guiding and multimodal electrophysiologic techniques has come into question in patients with cortical, spinal, and cerebellopontine angle (CPA) tumors (1,2,3,4). Intraoperative somatosensory-evoked potential (SEP), motor-evoked potential (MEP), brainstem-evoked potential (BAEP), visual-evoked potential, direct wave (D wave) assignment and continuous free muscle electromyography (EMG) are the most common multimodalities.

In this study, we planned to discuss the contribution of this practice to morbidity by considering tumor surgeries with intraoperative IONM based on our 4 years' experience.

Materials and Methods

Patients

Clinical, neurologic examination, neuroimaging study records, and follow-up information of all patients who underwent tumor surgery that required IONM between February 2012 and February 2016 were evaluated retrospectively for each patient. Tumor locations were divided into two regions; brain-located tumors and spinal-localized tumors.

Intraoperative Neurophysiologic Studies

Intraoperative neurophysiologic neuromonitorization of each patient was examined with monitoring protocols established using a 16-channel Viasys Nicolet Endeavor device. The use of multimodalities for IONM was decided according to the tumor location of each patient. All electrophysiologic changes and events that occurred during the operation were recorded. Total intravenous anesthesia (remifentanyl/propofol) was used as general anesthetic for all patients who were monitored. Neuromuscular blocking drugs were not used as anesthetic except for induction. Intraoperative blood pressure was recorded every ten minutes and values below 90 mmHg were recorded.

Intraoperative Motor-Evoked Potential Monitoring

MEP records were made using dual subdermal needle electrodes placed in the target muscle for each patient. Transcranial C1, C2, C3 and C4 regions/positions were preferred according to the international 10-20 system in terms of achieving the lowest threshold value for transcranial electrical stimulation. Corkscrew monopolar electrodes were placed under the scalp for stimulation. Each MEP response was monitored without averaging using a 5-stimuli train with an interstimulus interval of 4 msec. Filter ranges were set to 30-500 Hz, sweep time to 100 ms, and amplitude to 200 μ V. The negative and positive peak values of amplitudes of MEP responses were marked and monitored. A volume conductivity test was performed. MEP stimulation threshold intensity was determined for each muscle. A stimulation intensity of 1.5-2 fold the threshold intensity was applied throughout the surgery so as not to shake the patient and this stimulation intensity was not changed throughout the surgery.

Intraoperative Somatosensory-Evoked Potential Monitoring

Intraoperative SEP monitors stimulation of the median nerve in the upper extremities and posterior tibial nerve in the lower extremities. Peripheral nerve stimulation was obtained using dual-needle electrodes with a stimulation time of 0.5 ms. SEP records were made using scalp corkscrew electrodes placed on the C3'-Fz and C4'-Fz region for the upper extremities and the Cz'-Fz region for the lower extremities. Obtained records were monitored using the averaging system. Filter ranges were set to 30/500-1000 Hz. A 50% reduction in the amplitude of SEP, a 10% increase in latency period, total loss of muscle MEP or doubling of the stimulation threshold, which were used as critical criteria in previously published studies, were also used in this study (5,6,7,8).

Free Muscle Electromyography Recording Monitoring

Continuous free muscle EMG recording was performed using intramuscular double-needle electrodes. The sensitivity was set at 50 microvolts/D and filters at 3 Hz-1 kHz. Responses to stimulation performed using a peripheral nerve monopolar stimulator during the operation were monitored in required cases.

Intraoperative Brainstem-Evoked Potential Monitoring

BAEP values were obtained using both-ear stimulation and recording. Recordings were performed applying noise in one ear and 103 dB stimulation with a frequency of 17.5/11.1 Hz in the other ear. Recording channels were identified as Cz-A1 and Cz-A2 using subcutaneous monopolar electrodes (A1 and A2) placed in front of the tragus. The filter intervals were set to 5/3000 Hz, sweep time to 10 ms, and amplitude to 1 μ V/D.

Intraoperative Somatosensory-Evoked Potential Phase Reversal Procedure

SEP phase-reversal recordings were made using 6 or 8 monopolar strip electrodes placed perpendicular to the region on the cortical surface where the surgeon planned the area to be the central sulcus. The median nerve was stimulated and SEP responses on each superficial electrode were examined. After the procedure was over, the position of the recording electrode was changed by the surgeon and the procedure was repeated. Central sulcus localization was performed by monitoring the phase reversal of the cortical N20 wave obtained in this way.

Results

Clinical and Radiologic Evaluation

A total of 28 tumor surgeries were monitored between 2012 and 2016. The age range of the patients was 28-73 years; 11 were male (39.2%) and 17 were female (61.8%). The tumor location was spinal in 11 patients (39.2%), CPA in 28 patients (28.5%), and cortical and subcortical cranial in 9 patients (32.1%). The demographic characteristics and tumor location of the patients are given in Table 1. Preoperative neurologic examinations of 7 (25%) patients were within normal limits. Twenty-one (75%) patients had preoperative positive neurologic examinations.

Evaluation of Intraoperative Monitorization

Intraoperative monitoring modalities used according to the surgery type are presented in Table 1. Neurophysiologic changes

Table 1. Demographic characteristics, tumor location, and intraoperative monitoring modalities of patients

Patient number	Age	Sex	Tumor location	Modalities
1	35	F	Left frontoparietal	SEP, f EMG, corticography
2	43	M	Left sylvian	MEP, SEP, f EMG
3	73	M	Left temporal	SEP, f EMG, SEP phase reversal
4	38	F	Left frontal	SEP, f EMG, SEP phase reversal, corticography
5	38	M	Right frontotemporal	MEP, SEP, f EMG
6	41	F	Left sylvian	MEP, SEP, f EMG
7	28	F	Left caudate nucleus	MEP, SEP, f EMG
8	36	M	Left frontoparietal	MEP, SEP, f EMG
9	56	F	Right temporal	MEP, SEP, f EMG
10	47	F	Right cerebellopontine angle	MEP, SEP, f EMG, BAEP
11	34	F	Right cerebellopontine angle	MEP, SEP, f EMG, BAEP
12	52	F	Left cerebellopontine angle	MEP, SEP, f EMG, BAEP
13	56	F	Right cerebellopontine angle	MEP, SEP, f EMG, BAEP
14	30	M	Right cerebellopontine angle	MEP, SEP, f EMG, BAEP
15	37	M	Left cerebellopontine angle	MEP, SEP, f EMG, BAEP
16	42	M	Right cerebellopontine angle	MEP, SEP, f EMG, BAEP
17	33	M	Left cerebellopontine angle	MEP, SEP, f EMG, BAEP
18	62	F	Cervical 7-Thoracic 1	MEP, SEP, f EMG
19	38	M	Cervical 4-5	MEP, SEP, f EMG
20	54	F	Thoracic 5-6	MEP, SEP, f EMG
21	39	F	Thoracic 4-6	MEP, SEP, f EMG
22	23	F	Cervical 3-4	MEP, SEP, f EMG
23	48	F	Thoracic 10-11	MEP, SEP, f EMG
24	36	M	Cervical 4-5	MEP, SEP, f EMG
25	53	M	Lumbar 1-2	MEP, SEP, f EMG
26	46	F	Thoracic 2-3	MEP, SEP, f EMG
27	62	F	Thoracic 9-10	MEP, SEP, f EMG
28	51	F	Cervical 3-4	MEP, SEP, f EMG

MEP: Motor-evoked potential, SEP: Somatosensory-evoked potential, f EMG: Continuous free muscle electromyography, BAEP: Brainstem-evoked potential, F: Female, M: Male

Table 2. Patients with neurophysiologic changes

Patient number	Age	Sex	Tumor location	Neurophysiologic change observed during operation	Post-operative day 1 neurologic loss
2	43	M	Left sylvian	Decrease in SEP amplitudes (during resection)	None
5	38	M	Right frontotemporal	Temporary decrease in MEP, SEP amplitudes (Hypotension)	None
10	47	F	Right CPA	Temporary loss of MEP (Hypotension)	None
14	30	M	Right CPA	Decreased SEP and MEP amplitude	Right peripheral facial paralysis
15	37	M	Left CPA	Temporary elongation at BAEP latency	None

CPA: Cerebellopontine angle, SEP: Somatosensory-evoked potential, MEP: Motor-evoked potential, BAEP: Brainstem-evoked potential, F: Female, M: Male

were observed in 5 patients (17.8%) (Patients 2, 5, 10, 14, 15) (Table 2). Of these changes, 1 (3.5%) showed continuity (Patient 14). In this patient, bleeding occurred at the surgical site during tumor resection and progressive reduction started to be observed in MEP amplitude at the 3rd hour of surgery. Instant changes due to irritation in the facial muscles were observed in the free EMG panel. A decrease in the amplitude of SEP potential was observed. The surgical team was warned when a critical level was reached, but the surgery continued because of difficulty in resection and continuation of the bleeding. The same patient was monitored for BAEP, but although BAEP potentials were recorded, the monitoring was performed by MEP, SEP, and free EMG because the patient had hearing loss in the preoperative period. Intraoperative changes detected in 4 (14.2%) other patients were transient and were corrected following correction of hypotension parameters. The loss of SEP potentials and vasoconstriction during tumor resection in one patient were simultaneous and SEP potentials were improved after the resection.

Functional and Monitoring Evaluation

The postoperative neurologic status of the patients was evaluated on day 1 and day 15. No change was observed in 24 (85.7%) patients on postoperative day 1. Four patients (14.2%) (Patients 5, 13, 14, 17) developed new neurologic deficits after surgery. One of these patients had a frontotemporal tumor and 3 had CPA tumors; a permanent deficit was observed in only one patient at the end of the 15th day. The patient with frontotemporal tumor was followed up in the continuous care unit by the neurosurgery clinic because of septic shock in the postoperative period. The intraoperative evaluations of the patients with neurologic deficits are given in Table 3.

Discussion

IONM, which is increasingly used in our country and around the world, is used to minimize surgical morbidity. Tumors located in critical anatomic locations have increased its importance due to its sensitivity in surgical interventions during resection, and its use has often come into question. IONM was performed during tumor surgery in 28 neurosurgery patients at our center during the defined period. The different modalities of IONM vary according to the case and tumor location, and multimodal monitoring was preferred. Although the specificity of MEP monitoring used during IONM is higher than that of SEP monitoring, the specificity in multimodal dual use reaches up to 100% (8,9,10,11,12,13,14,15).

The well-known limitations of this method are blood pressure, temperature, and partial alveolar carbon dioxide pressure; these affect the waveform of IONM (16). Neurophysiologic changes during IONM are known to develop during tumor resection (3,17,18). However, IONM is recommended from the beginning to the end of the surgery because of the possibility of neurophysiologic changes before resection.

The fact that the data were observed in a single center, in a small group of patients, and retrospectively is a limitation of this study. Multi-center studies involving larger patient groups should be among future targets. Furthermore, despite the fact that 10 spinal cord tumor surgeries were monitored in our series, the absence of D wave monitorization is another limitation of the study. The importance of monitorization of D wave, especially during cervical and thoracic tumor resection, has been emphasized in the literature; motor deficits due to surgery would be transient if the D wave is sustained or the loss of amplitude is not more than 50% despite the loss of muscle MEPs during tumor resection, thus surgery could be continued (3). In a study by Ilgaz Aydınlar et al. (19) in Turkey, surgery for spinal tumor was continued in a case in which there was a 30% decrease in amplitude of D-wave despite the disappearance of MEP, and the patient was finally discharged without deficit. There were no false positive or false negative results in our study. False positive results can lead to harmful and unnecessary treatment with economic burden (20,21). False negative results have not been reported frequently in the literature.

It is known that there is a relationship between tumor size and development of hearing loss during resection of CPA tumors (22). In our series, patient 14 had hearing loss pre- and post-operatively. There was no clear interpretation of cranial 8th nerve injury in the patient, who had peripheral facial paralysis. Deficit development was thought to be associated with bleeding complications during tumor surgery.

Based on the results of our study, we think that multimodal monitorization with SEP and MEP during all central nervous system tumor surgeries can predict surgery-related neurologic complications such as paraparesis, paraplegia and quadriplegia, and provide more reliable surgery for surgeons.

Conclusion

Besides surgical technique, anesthetic applications and imaging, intraoperative neuromonitorization is a method that should be performed in surgical procedures involving critical

Table 3. Patients with post-operative worsening neurologic examination

Patient number	Age	Sex	Tumor location	Used modalities	Post-operative day 1 neurologic loss	Post-operative day 15 neurologic loss
5	38	M	Right frontotemporal	MEP, SEP, BAEP, f EMG	Unconscious, quadriplegic (septic shock)	Normal
13	56	F	Right CPA	MEP, SEP, BAEP, f EMG	Mild right peripheral facial paralysis	Normal
14	30	M	Right CPA	MEP, SEP, BAEP, f EMG	Severe right peripheral facial paralysis	Right peripheral facial paralysis
17	33	M	Left CPA	MEP, SEP, BAEP, f EMG	Mild left peripheral facial paralysis	Normal

CPA: Cerebellopontine angle, MEP: motor-evoked potential, SEP: Somatosensory-evoked potential, BAEP: Brainstem-evoked potential, f EMG: Continuous free muscle electromyography, F: Female, M: Male

anatomic structures. These monitoring techniques should be used together when necessary, and surgical morbidity should be minimized.

Ethics

Ethics Committee Approval: The study does not need of ethics committee approval. The paper does not report on the use of experimental or new protocols. All data analyzed were collected as part of routine diagnosis and treatment.

Informed Consent: No need of informed consent.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.I.T., M.M., F.G.Y., K.V., Concept: F.G.Y., K.V., Design: F.G.Y., K.V., Data Collection or Processing: F.G.Y., K.V., Analysis or Interpretation: F.G.Y., K.V., Literature Search: F.G.Y., K.V., Writing: F.G.Y.

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References

- Deletis V, Sala F. Intraoperative neurophysiological monitoring of the spinal cord during spinal cord and spine surgery: a review focus on the corticospinal tracts. *Clin Neurophysiol* 2008;119:248-264.
- Nuwer MR. Overview and history. In: Daube JR, Mauguière F, Nuwer MR (eds). *Handbook of clinical neurophysiology, intraoperative monitoring of neural function* New York, NY: Elsevier, 2008:2-6.
- Sala F, Palandri G, Basso E, Lanteri P, Deletis V, Faccioli F, Bricolo A. Motor evoked potential monitoring improves outcome after surgery for intramedullary spinal cord tumors: a historical control study. *Neurosurgery* 2006;58:1129-1143.
- Sala F, Dvorak J, Faccioli F. Cost effectiveness of multimodal intraoperative monitoring during spine surgery. *Eur Spine J* 2007;16:229-231.
- Deletis V. Intraoperative monitoring of the functional integrity of the motor pathways, in Devinsky O, Beric A, Dogali M (eds). *Electrical and Magnetic stimulation of the Brain and spinal cord*. New York: Raven Press, 1993:201-214.
- Kothbauer K, Deletis V, Epstein FJ. Intraoperative spinal cord monitoring for intramedullary surgery: an essential adjunct. *Pediatr Neurosurg* 1997;26:247-254.
- Sala F, Lanteri P, Bricolo A. Motor evoked potential monitoring for spinal cord and brain stem surgery. *Adv Tech Stand Neurosurg* 2004;29:133-169.
- Kelleher MO, Tan G, Sarjeant R, Fehlings MG. Predictive value of intraoperative neurophysiological monitoring during cervical spine surgery: a prospective analysis of 1055 consecutive patients. *J Neurosurg Spine* 2008;8:215-221.
- Eager M, Shimer A, Jahangiri FR, Shen F, Arlet V. Intraoperative neurophysiological monitoring (IONM): lessons learned from 32 case events in 2069 spine cases. *Am J Electroneurodiagn Technol* 2009;51:247-263.
- Hilibrand AS, Schwartz DM, Sethuraman V, Vaccaro AR, Albert TJ. Comparison of transcranial electric motor and somatosensory evoked potential monitoring during cervical spine surgery. *J Bone Joint Surg Am* 2004;86:1248-1253.
- Khan MH, Smith PN, Balzer JR, Crammond D, Welch WC, Gerszten P, Scلابassi RJ, Kang JD, Donaldson WF. Intraoperative somatosensory evoked potential monitoring during cervical spine corpectomy surgery: experience with 508 cases. *Spine* 2006;31:105-113.
- Quraishi NA, Lewis SJ, Kelleher MO, Sarjeant R, Rampersaud YR, Fehlings MG. Intraoperative multimodality monitoring in adult spinal deformity: analysis of a prospective series of one hundred two cases with independent evaluation. *Spine (Phila Pa 1976)* 2009;34:1504-1512.
- Matsuyama Y, Sakai Y, Katayama Y, Imagama S, Ito Z, Wakao N, Sato K, Kamiya M, Yukawa Y, Kanemura T, Yanase M, Ishiguro N. Surgical results of intramedullary spinal cord tumor with spinal cord monitoring to guide extent of resection. *J Neurosurg Spine* 2009;10:404-413.
- Kobayashi S, Matsuyama Y, Shinomiya K, Kawabata S, Ando M, Kanchiku T, Saito T, Takahashi M, Ito Z, Muramoto A, Fujiwara Y, Kida K, Yamada K, Wada K, Yamamoto N, Satomi K, Tani T. A new alarm point of transcranial electrical stimulation motor evoked potentials for intraoperative spinal cord monitoring: a prospective multicenter study from the Spinal Cord Monitoring Working Group of the Japanese Society for Spine Surgery and Related Research. *J Neurosurg Spine* 2014;20:102-107.
- Quiñones-Hinojosa A, Lyon R, Zada G, Lamborn KR, Gupta N, Parsa AT, McDermott MW, Weinstein PR. Changes in transcranial motor evoked potentials during intramedullary spinal cord tumor resection correlate with postoperative motor function. *Neurosurgery* 2005;56:982-993.
- Ziewacz JE, Berven SH, Mummaneni VP, Tu TH, Akinbo OC, Lyon R, Mummaneni PV. The design, development, and implementation of a checklist for intraoperative neuromonitoring changes. *Neurosurg Focus* 2012;33:E11.
- Garcés-Ambrossi GL, McGirt MJ, Mehta VA, Sciubba DM, Witham TE, Bydon A, Wolinsky JP, Jallo GI, Gokaslan ZL. Factors associated with progression-free survival and long-term neurological outcome after resection of intramedullary spinal cord tumors: analysis of 101 consecutive cases. *J Neurosurg Spine* 2009;11:591-599.
- Jenkinson MD, Simpson C, Nicholas RS, Miles J, Findlay GF, Pigott TJ. Outcome predictors and complications in the management of intradural spinal tumours. *Eur Spine J* 2006;15:203-210.
- İlgaz Aydınlar E, Yalınay Dikmen P, Silav G, Berkman MZ, Elmacı İ, Özgen S. Intraoperative Neurophysiological Monitoring to Prevent New Neurological Deficits in Spinal Tumor Cases. *Turk J Neurol* 2014;20:47-50.
- Langeloo DD, Lelivel A, Louis Journee H, Slappendel R, de Kleuver M. Transcranial electrical motor-evoked potential monitoring during surgery for spinal deformity: a study of 145 patients. *Spine (Phila Pa 1976)* 2003;28:1043-1050.
- Skinner SA, Holdefer RN. Intraoperative neuromonitoring alerts that reverse with intervention: treatment paradox and what to do about it. *J Clin Neurophysiol* 2014;31:118-126.
- Wiet RJ, Mamikoglu B, Odom L, Hoistad DL. Long-term results of the first 500 cases of acoustic neuroma surgery. *Otolaryngol Head Neck Surg* 2001;124:645-651.