Characterization of intraoperative motor evoked potential monitoring for pediatric brain tumor surgery

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Running title: Characterization of MEP for pediatric brain tumor surgery

Keywords: motor evoked potentials, transcortical MEP, direct cortical stimulation, children, brain tumor surgery

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Abstract

Objective

To investigate the relationship between the reliability of the transcranial or transcortical motor evoked potential (MEP) response and age in patients less than 15 years of age with pediatric brain tumor.

Methods

We retrospectively analyzed data from 60 consecutive patients under the age of 15 years who underwent brain tumor surgery that involved intraoperative MEP monitoring between October 2009 and May 2016.

Results

In total, there were 41 patients with reliable signals (MEP response group) and 19 patients without reliable signals (MEP non-response group). The mean age at surgery, body height, and body weight were significantly greater in the MEP response group than in the MEP non-response group.

When the MEP success rates during pediatric brain tumor surgery were analyzed in relation to patient age, the transcortical MEP success rate of the 0- to 5-year age group (10.0%) was significantly lower than that of the 6- to 10-year age group (71.4%) ($p = 0.009$) and that of the 11- to 15-year age group (75.0%) ($p = 0.015$).

Conclusions

In summary, the transcortical MEP response was monitored less successfully during brain tumor surgery in patients less than 5 years of age than in patients between the ages of 6 and 15 years. Although MEP monitoring techniques can be applied in pediatric brain tumor surgery as they are for adult patients, the limitations of the low transcortical MEP response rate in young patients should be considered.

Introduction

The recent improvement in modern surgical modalities such as intraoperative neurophysiological monitoring[1], intraoperative magnetic resonance imaging (iMRI)[2,3], and neuronavigation systems[4], have increasingly enabled more aggressive tumor resections, even in tumors observed near or in eloquent areas of the brain. In particular, motor evoked potentials (MEP), including transcranial and transcortical MEP, are beneficial for identifying motor fibers while performing surgery in close proximity to the motor cortex and/or corticospinal pathway[4,5]. The goal of brain tumor surgery is to

achieve maximal tumor resection while preserving brain function, e.g., motor function; therefore, its improvement could optimize the clinical outcome of patients with brain tumors and ultimately increase patient quality of life. As recent advances in both anesthetic and electrophysical monitoring techniques have led to an improvement in the reliability of MEP monitoring[6-10], it has the potential to decrease the significant risk of neurological impairment, especially severe motor deficit, that is associated with brain tumor surgery.

However, though MEP monitoring techniques have been well established in adult patients, its efficacy and reliability in pediatric brain tumor patients has not yet been defined. Furthermore, the reliability of MEP in relation to the age of children with intracranial tumor remains unknown, though previous reports have shown the data of only transcranial MEP monitoring elicited by transcranial electric stimulation in pediatric spine surgery patients[6,11,12]

In the current study, we aimed to investigate and describe the relationship between the reliability of transcranial or transcortical MEP response and age in patients under the age of 15 years with pediatric brain tumor. Moreover, the success rate of MEP monitoring was evaluated from a series of 60 consecutive surgeries performed in children with brain tumors under the age of 15 years. Of these, we assessed the responses rate of transcranial or transcortical MEP in pediatric brain tumor patients.

Materials & Methods

Patient Cohorts

Data from all children under 15 years of age (range: 0-15 years) who underwent brain tumor surgery that attempted intraoperative MEP monitoring at Nagoya University Hospital between October 2009 and May 2016 were consecutively investigated in the present study. All patients were diagnosed with brain tumors, including supratentorial and infratentorial tumors, by preoperative magnetic resonance imaging (MRI) (Table 1). Two expert neuropathologists independently established the histological diagnosis of brain tumor in accordance with the 2007 or 2016 World Health Organization (WHO) classification[13 14-16]. The institutional review board/ethics committee at Nagoya University Hospital approved the study (approval number: 2016-0411), and written informed consent was obtained from all patients or their legal guardians.

Intraoperative MEP monitoring protocol

MEP was obtained using transcranial or transcortical electrical stimulation. In all patients, the Neuromaster MEE1200 (Nihon Kohden, Tokyo, Japan) was used for intraoperative neurophysiological monitoring during brain tumor surgery. Transcortical MEP was used for tumors

located close to the primary motor cortex. First, somatosensory evoked potential (SEP) with N-20 phase reversal were examined using a strip electrode to identify the central sulcus. Next, transcortical MEP was elicited with a short train of high frequency anodal stimulation applied with a strip electrode on the precentral gyrus (500 Hz, duration: 0.4 ms, train: 5, 20-40 mA). Muscle action potentials were recorded in the contralateral upper and lower extremities, including the biceps, abductor pollicis brevis, tibialis anterior, and abductor hallucis.

In cases in which we determined that we would not be able to place the electrode on the primary motor area, we performed transcranial MEP monitoring during removal of the brain tumor. In addition, the patients who we performed transcortical MEP monitoring did not take simultaneous transcranial MEPs. Transcranial electrical MEP was recorded over the bilateral upper and lower extremities on the abductor pollicis brevis and abductor hallucis muscles following a short train of high frequency anodal electrical stimulation (500 Hz, duration: 0.5 ms, train: 5, 80-180 mA). MEP stimulation was delivered through two corkscrew scalp electrodes (Medotronic, Goleta, CA) placed over regions of the motor cortex under the guidance of a intraoperative neuronavigation system that used the iPlan® cranial planning software included in BrainLAB iPlan® Cranial 3.0 (BrainLAB, Feldkirchen, Germany)[17]. All patients were evaluated for transcortical or transcranial MEP responses by expert medical technologists (K.S or C.T) throughout the entire study. Maximum amplitudes were not used because the important factor associated with the MEP monitoring is the stability of the responses. Thus, the criteria for reliable responses was determined as follows: at least 75% of the MEPs should have an amplitude of 25μV during the whole period. MEPs were recorded at least every 5 minutes during the surgical procedure.

Anesthesia

Anesthesia was maintained with propofol (50-100 μg/kg/minute) and remifentanyl citrate in all patients. A muscle relaxant was not used. During the microsurgical procedure, transcortical stimulation was performed periodically at intervals of 30-120 seconds.

Statistical analysis

The Mann-Whitney U test, Student's t-test, $\chi 2$ test, and Fisher's exact test were used to test the association of clinical variables between the groups. Statistical analyses were performed using the statistical software, IBM SPSS Statistics for Windows, version 24.0 (IBM Corporation, Armonk, NY). A p value < 0.05 was considered statistically significant.

Results

Clinical characteristics

As summarized in Table 1, 60 consecutive patients under the age of 15 years who underwent tumor resection for intracranial tumors between October 2009 and May 2016 were registered in the present study. Thirty-eight male and 22 female participants, ranging in age from 0 to 15 years (median age: 8 years) were included. The patients' mean body height was 127.7 cm (range: 59-179.2 cm) and their mean body weight was 24.3 kg (range: 5.7-58.1 kg). Histologically, this study included 28 gliomas, 3 meningiomas, 4 medulloblastomas, 10 ependymomas, 7 germ cell tumors, 3 craniopharyngiomas, and 2 angiomas. The brain tumors were diversely located, and included 11 frontal, 8 temporal, 2 parietal, 2 insular, 5 thalamic, 3 suprasellar, 7 pineal, 4 cerebellar, 10 fourth ventricle, 2 third ventricle, 4 lateral ventricle, and 2 brainstem tumors. Motor potentials were evoked by means of transcranial high-frequency cortex stimulation in 38 patients and transcortical stimulation in 22 patients. The decision to use transcranial or transcortical MEP was based on tumor location.

Basic characteristics of the MEP response and non-response groups

Among the 60 patients, 41 patients had reliable signals (MEP response group) and 19 patients had unreliable signals (MEP non-response group). The main baseline clinical characteristics of the MEP response and non-response groups are summarized in Table 2. The mean age at surgery was significantly higher in the MEP response group (9.3 ± 3.7 years) than in the MEP non-response group (5.2 ± 3.8 years) ($p < 0.001$). The MEP response and non-response groups consisted of 70.7% and 47.4% male patients, respectively. The mean body height of the MEP response group was significantly higher, at 135 ± 23 cm, than that of the MEP non-response group, at 108 ± 27 cm ($p < 0.001$). Similarly, the mean body weight in the MEP response group (31 ± 12 kg) was significantly greater than that of the MEP non-response group (22 ± 14 kg) ($p < 0.01$). The difference in preoperative motor deficit between the two groups, as determined by a Fisher's exact test, was not statistically significant. Notably, when transcranial MEP was performed, the mean stimulation amplitude of the MEP response group (113 ± 39 mA) was lower than that of the MEP non-response group (171 ± 39 mA) ($p < 0.001$). The mean stimulation amplitudes used for transcortical MEP were 29 ± 3 mA and 29 ± 6 mA for the MEP response and non-response groups, respectively. There is no association between MEP response and tumor location, pathology in this study. All patients in MEP response group had a favorable neurological motor outcome (without motor deficits) after tumor removal.

Success rates of MEP during pediatric brain tumor surgery in relation to patient age

Overall, the transcranial, transcortical, and total (transcranial or transcortical) MEP success rates were 82.1%, 42.9%, and 68.3%, respectively (Table 3). Success rates for transcranial and transcortical MEP in relation to patient age (0-5, 6-10, and 11-15 years) are shown in Table 3. The 0- to 5-year age group, 6- to 10-year age group and 11- to 15-year age group consisted of 18, 22 and 20 patients, respectively. Although the transcranial MEP success rate was not significantly affected by age, the transcortical MEP success rate of the 0- to 5-year age group (10.0%) was significantly lower than that of the 6- to 10-year age group (71.4%) ($p = 0.009$) and that of the 11- to 15-year age group (75.0%) ($p = 0.015$). There was no statistically significant difference between the 6- to 10-year age group (71.4%) and the 11- to 15-year age group (75.0%) in terms of transcortical MEP success rate. The total transcranial or transcortical MEP success rate in the 0- to 5-year age group (33.3%) was significantly lower than that of the 6- to 10-year age group (77.3%) ($p = 0.005$) and that of the 11- to 15-year age group (90.0%) ($p = 0.0003$).

Discussion

Intraoperative monitoring of MEP for the prevention of postoperative motor impairments is an established technique in adult brain tumor patients[18-21]. MEP can be elicited through either transcortical or transcranial electrical stimulation. Some studies involving the monitoring of transcortical MEP during the resection of intracranial tumors have found there to be an association between a reduction in amplitude greater than 50-80% and the loss of the MEP response[18-21]. However, the use of MEP with reliable signals in a pediatric population differs substantially from that of the adult population during brain tumor surgery.

Although few studies have reported on the intraoperative monitoring of MEP in children during brain tumor surgery, our results revealed that reliable signals are difficult to detect in the MEP response in patients less than 5 years of age when standard anesthesia techniques are used. Specifically, the recording of reliable transcortical MEP was less successful in the 0- to 5-year age group (10.0%) than in the 6- to 10-year age group (71.4%) or the 11- to 15-year age group (75.0%) (Table 3). These results are consistent with previous reports[1,22-24]. To date, it has been reported that the success rate of MEP is low in neurologically normal children under the age of 7 years[22-24]. The major reason for the low success rate of transcortical MEP recordings in the present study is assumed to be due to the electrophysiologic immaturity of the corticospinal tract, which is generally not considered mature until approximately 10 years of age[22,24]. Additionally, the myelinization of the corticospinal tract continues throughout early childhood, further explaining the age-related MEP responses found in the present study.

On the other hand, the transcranial MEP success rate in the 0- to 5-year age group (62.5%) was not significantly different from that of the 6- to 10-year age group (80.0%) or the 11- to 15-year age group (93.8%) (Table 3). Since higher intensity stimulation was required in transcranial MEP than in transcortical MEP (20-40 mA vs. 80-180 mA), there is a possibility that not only areas such as the corticospinal tract, but also deeper levels such as the brainstem[25], were activated. This might have altered the transcranial MEP success rate to increase in the 0- to 5-year age group. Furthermore, the immaturity of the corticospinal tract in very young children may have increased the required MEP stimulation thresholds. In such a situation, the corticospinal tract might be activated distally to the level of the subcortical injury, thus producing a false negative response in younger children with brain tumors. For these reasons, we thought that they were less able to obtain reliable recordings by direct cortical stimulation in the youngest cohort compared to the older patients, but that there was no difference according to the age in pediatric patients elicited by transcranial electrical stimulation.

We used propofol and remifentanil as the standard anesthetic technique for all 60 patients during electrophysiologic testing during brain tumor surgery. Soriano et al. previously demonstrated that propofol did not interfere with intraoperative electrocorticography or cortical stimulation for language tasks during awake brain mapping in children 11- to 15-years of age. Although it is possible that propofol had a dose-dependent depressive effect on MEP[26,27], no differences of propofol dose between the MEP response and MEP non-response groups were found in the current study.

This report provides novel information on the transcortical and transcranial MEP success rates during pediatric brain tumor surgery in relation to patient age; however, our findings are limited in comparison with those of prospective clinical trials, as retrospective studies can be influenced by unrecognized biases. Furthermore, this report was based on a small number of cases; therefore, a larger cohort study is required to further establish the role of transcortical and transcranial MEP in children under the age of 15 years. Additional evidence from transcortical and transcranial MEP is crucial to improve our understanding of intraoperative motor function assessment during pediatric brain tumor surgery.

Conclusions

In summary, the transcortical MEP response was not successfully monitored during brain tumor surgery in patients less than 5 years of age in comparison with patients between 6 and 15 years of age. Although the same MEP monitoring techniques can be applied in pediatric brain tumor surgery as in adult surgery, the limitation of the low transcortical MEP response rate in young patients, which

likely occurs as a result of corticospinal tract immaturity, should be better understood.

Acknowledgments

The authors would like to thank Ms. Chiaki Tsutsumi, Ms. Aiko Okuma, Ms. Saryong Kim, and Mr. Hiroyuki Matsumoto (Department of Medical Technique, Nagoya University Hospital, Nagoya, Japan) for their wonderful technical assistance.

Disclosure Statement

Kazuya Motomura was supported by grants from a Grant-in-Aid (C) for Scientific Research from the Ministry of Health, Labor, and Welfare of Japan. The authors have no conflicts of interest to declare in this study.

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Table 1. Clinical characteristics

Parameters		No. of patients (n=60)	%
Age (yrs)			
	Median	8	
	Range	0-15	
Sex			
	Male	38	63.3
	Female	22	36.7
Body height (cm)			
	Mean	127.7	
	Range	59-179.2	
Body weight (kg)			
	Mean	24.3	
	Range	5.7-58.1	
Tumor type			
	Glioma	28	46.7
	Meningioma	3	5.0
	Medulloblastoma	4	6.7
	Ependymoma	10	16.7
	Germ cell tumor	7	11.7
	Craniopharyngioma	3	5.0
	Angioma	2	3.3
	Others	3	5.0
Tumor location			
	Frontal	11	18.3
	Temporal	8	13.3
	Parietal	2	3.3
	Insular	2	3.3
	Thalamus	5	8.3
	Suprasellar	3	5.0
	Pineal	7	11.7
	Cerebellum	4	6.7
	Fourth ventricle	10	16.7
	Third ventricle	2	3.3
	Lateral ventricle	4	6.7
	Brain stem	2	3.3
MEP			
	Transcranial	38	63.3
	Transcortical	22	36.7

Abbreviation: MEP; motor evoked potential

Table 2. The basic characteristics associated with brain tumor surgery in children

Mean ± SD

	All patients (n=60)		MEP response group (with reliable signals) (n=41)	MEP non-response group (with no reliable signals) (n=19)	*P* value
Mean age (years)	8.0±4.2		9.3±3.7	5.2±3.8	＜0.001
Male/ female	38/22		29/12	9/10	
Mean body height (cm)	126±27		135±23	108±27	＜0.001
Mean body weight (kg)	28±14		31±12	22±14	＜0.01
Preoperative motor deficit					
(+)	14		8	3	*
(-)	46		33	13	
Transcranial/Transcortical MEP	39/21		32/9	7/12	
Mean stimulation amplitude (mA)					
Transcranial MEP	123±45		113±39	171±39	＜0.001
Transcortical MEP	29±5		29±3	29±6	**

Abbreviation: MEP; motor evoked potential

*Fisher's exact test >0.05

** t-test>0.05

Table 3. Comparison of the MEP success rates during pediatric brain tumor surgery in relation to the age

	MEP success rates (%)		
	Transcranial MEP	Transcortical MEP	Transcranial/Transcortical MEP
Age (years)			
0-5 (n=18)	62.5 (5/8)	10.0[a) b)] (1/10)	33.3[c) d)] (6/18)
6-10 (n=22)	80.0 (12/15)	71.4[a)] (5/7)	77.3[c)] (17/22)
11-15 (n=20)	93.8 (15/16)	75.0[b)] (3/4)	90.0[d)] (18/20)
Total (n=60)	82.1 (32/39)	42.9 (9/21)	68.3 (41/60)

Abbreviation: MEP; motor evoked potential

a), b), c), d) Significantly different ($p<0.05$) between two groups, respectively