Intraoperative corticomuscular motor evoked potentials for evaluation of motor function: a comparison with corticospinal D and I waves

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Object. The goal of this study was to compare motor evoked potentials recorded from muscles (muscle MEPs or corticomuscular MEPs) with corticospinal MEPs recorded from the cervical epidural space (spinal MEPs or corticospinal MEPs) to assess their efficacy in the intraoperative monitoring of motor function.

Methods. Muscle and spinal MEPs were simultaneously recorded during surgery in 80 patients harboring brain tumors. Each case was assigned to one of four groups according to final changes in the MEPs: 1) Group A, in which there was an increased amplitude in the muscle MEP with an increased I3 wave amplitude (12 cases); 2) Group B, in which there was no significant change in the MEP (43 cases); 3) Group C, in which there was a decreased muscle MEP amplitude (< 35% of the control) with a decreased I wave amplitude but an unchanged D wave (15 cases); or 4) Group D, in which there was an absent muscle MEP with a decreased D wave amplitude (10 cases). In patients in Group A, the increase in the amplitude of the muscle MEP (range of increase 128–280%, mean increase 188.75 ± 48.79%) was well correlated with the increase in the I3 wave in corticospinal MEPs. Most of these patterns were observed in patients harboring meningiomas (10 [83.3%] of 12 cases). Patients in Group B displayed no changes in muscle and corticospinal MEPs and no signs of postoperative neurological deterioration. Patients in Group C showed a substantial decrease in the amplitude of the muscle MEP (range of decrease 5.3–34.8% based on the control waveform, mean change 21.81 ± 10.93%) without deterioration in the corticospinal D wave, and exhibited severe immediate postoperative motor dysfunction. This indicates dysfunction of the cortical gray matter, including the motor cortices, which are supposed to generate I waves. Patients in Group D exhibited decreases in the corticospinal D wave (range of decrease 21.5–55%, mean decrease 39.75 ± 11.45%) and an immediate cessation of the muscle MEP as well as severe permanent motor paresis.

Conclusions. These results indicate that, during surgery, monitoring of corticomuscular MEPs (which are related to I waves) is a much more sensitive method for the detection of immediate motor cortical damage than monitoring of corticospinal MEPs (D wave).

KEY WORDS • motor cortex • electrical stimulation • intraoperative monitoring • corticospinal D wave • corticospinal I wave • transcranial magnetic stimulation • motor evoked potential

The authors of several studies have demonstrated the validity of monitoring MEPs recorded from the spinal cord after electrical stimulation of the motor cortex while monitoring the function of the central motor pathways in humans. Corticospinal MEPs consist of a corticospinal D wave followed by two or three I waves (I1, I2, and I3 waves, respectively). The corticospinal D wave, evoked by direct activation of pyramidal axons, is known as the most reliable indicator of damage in intraoperative MEP monitoring. Recent advances in anesthesia and intraoperative stimulation techniques have made it possible to record MEPs from peripheral muscles (muscle MEPs). The clear advantage of this method lies in the ease and noninvasiveness of the recording procedure (there is no need for inserting cervical epidural electrodes). The literature contains many recent reports on the use of this technique for intraoperative motor function monitoring, however, few researchers have proposed a definite critical limit in muscle MEPs during intraoperative monitoring because of the variability in muscle MEPs during surgery. For example, postoperative motor performance can be preserved even after the transient disappearance of intraoperative muscle MEPs.

The primary purpose of this study was to clarify the relationships between alterations in corticospinal and muscle MEPs during surgery and the patient’s postoperative motor status. To elucidate the mechanism and pathophysiology of motor systems, we explored corticospinal descending systems under surgical conditions by using a simultaneous corticospinal and muscle MEP recording technique.

Clinical Material and Methods

All protocols were approved by the Oita University Eth-
ical Review Committee. Written informed consent was obtained from each patient for intraoperative monitoring, anesthesia, and the surgical procedure.

Patient Population

Intraoperative MEPs were studied in 80 patients (42 men and 38 women, age range 15–73 years [mean 60.3 ± 9.66 years]) who were undergoing surgery for brain tumors (GBM in 41 patients, WHO Grade III glioma in four patients, WHO Grade I or II [low-grade] glioma in 16 patients, meningioma in 12 patients, and metastasis in seven patients [Table 1]). Preoperatively, all these patients’ motor performances were fair (MMT Score 4–5).

Preoperative Identification of the Motor Cortex

Before the operation commenced, the cerebral motor cortex was stimulated and identified using a high-power magnetic stimulator (Magstim 200; Magstim Co., Whitland, Carmarthenshire, Wales, UK). A figure eight–shaped coil with an external loop diameter of 9 cm was held over the motor cortex at the scalp position considered optimal to elicit motor responses in the APB and other upper-extremity muscles. Intensities were expressed as percentages of the maximal output of the stimulator. The RMT was defined according to recommendations of the International Federation of Clinical Neurophysiology Committee17 as the minimal stimulus intensity necessary to produce a liminal MEP (~ 50 μV in 50% of trials) with the tested muscle at rest.

Motor evoked potentials were recorded at an intensity of 1.2 RMT from the relaxed APB muscle of the contralateral hand. The electromyography responses were amplified and filtered (bandwidth 3 Hz–3 kHz) using an evoked potential measuring system (Neuropack 8; Nihon Kohden Corp., Tokyo, Japan).

Intraoperative MEP Recording

As has been reported by Neuloh and associates,14 MEPs from the APB and other muscles adjacent to the tumor (the biceps brachii, brachioradialis, abductor digiti minimi, and first dorsal interosseous muscles with occasional supplementation by the anterior tibial and facial muscles) were simultaneously recorded both pre- and intraoperatively.

Intraoperative MEP monitoring from muscles was performed with the patient in a state of total anesthesia. Anesthesia was first induced in the patient by administering a mixture of propofol (1–2 mg/kg) and fentanyl (5–10 μg/kg/hr), and was maintained using a continuous intravenous injection of propofol (5–8 mg/kg/hr). Muscle relaxants were not administered except for intubation. Four plate electrodes (each 5 mm in diameter with a 10-mm center-to-center interelectrode distance; Unique Medical Co., Tokyo, Japan) were placed on the pial surface of the cerebral cortex after the cortex had been exposed. Direct electrical stimulation was applied to the cortex by using monopolar, monophasic anodal stimulation (short train of 500 Hz, four pulses) for identification of the motor cortex.11 The cathode used for monopolar stimulation was located ipsilaterally on either the Fp1 or Fp2 location according to the international 10–20 electroencephalography system. The stimulus used for recording was applied as a single monopolar, anodal, monophasic square wave pulse with a 0.2- to 0.5-msec duration and a 5- to 20-mA intensity (twice the threshold). Nonaveraged spinal and muscle MEPs were recorded through a 30- to 3000-Hz bandpass filter. The reproducibility of the MEPs was confirmed by checking at least two traces. Intraoperative identification of the central sulcus and the central region was made using a combination of somatosensory evoked potential phase reversal and direct monopolar, anodal, high-frequency electrical stimulation of the cortex.13 The site on the scalp corresponding to the APB muscle (APB point) was registered using a neuronavigation system (Nexstim eXimia, an image-guidance system based on three-dimensional computerized views [Nexstim Co., Helsinki, Finland] or the Viewing Wand system [ISG Technologies, Toronto, ON, Canada]) so that the restricted area of the motor cortex could be identified easily.8 The position of the anodal electrode on the cortical surface was initially set just under the APB point on each patient, and then adjusted to the site at which we could obtain the clearest MEPs simultaneously from the spinal epidural space and the muscles.

The corticospinal MEPs were recorded using bipolar epidural leads, which were inserted at the upper thoracic level and then advanced rostrally to record from the C-3 region under the control of x-ray imaging. Bipolar recording from this electrode, which consisted of five leads 8 mm apart (UKG-100-XPM; Unique Medical Co.), was conducted using two rostral and caudal site pairs.

During the operation, the muscle MEPs were recorded from the same muscle position in which definite muscle MEPs had been observed preoperatively. The APB muscle MEPs were chosen for pre- and intraoperative evaluation.

### TABLE 1

<table>
<thead>
<tr>
<th>Histological types and sites of lesions</th>
<th>No. of Cases (%)</th>
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<tbody>
<tr>
<td>GBM</td>
<td>41 (51.25)</td>
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<tr>
<td>glioma (WHO Grade III)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>low-grade glioma (WHO Grade I or II)</td>
<td>16 (20)</td>
</tr>
<tr>
<td>meningioma</td>
<td>12 (15)</td>
</tr>
<tr>
<td>metastasis</td>
<td>7 (8.75)</td>
</tr>
<tr>
<td>site of lesion</td>
<td></td>
</tr>
<tr>
<td>precentral</td>
<td>46 (57.5)</td>
</tr>
<tr>
<td>SMA</td>
<td>5 (6.25)</td>
</tr>
<tr>
<td>postcentral</td>
<td>7 (8.75)</td>
</tr>
<tr>
<td>precentral &amp; postcentral</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>insular &amp; striatum</td>
<td>20 (25)</td>
</tr>
</tbody>
</table>

### TABLE 2

<table>
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<tr>
<th>Latency and amplitude values of MEPs</th>
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<tr>
<td>Preoperative Control MEP Measurement</td>
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<tr>
<td>Parameter</td>
</tr>
<tr>
<td>latency (msec)</td>
</tr>
<tr>
<td>mean</td>
</tr>
<tr>
<td>SD</td>
</tr>
<tr>
<td>amplitude (μV)</td>
</tr>
<tr>
<td>mean</td>
</tr>
<tr>
<td>SD</td>
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</table>
because when they were used there was consistent simultaneous recording of spine and muscle MEPs and accurate identification of the motor cortex even under surgical conditions. Intraoperative MEP monitoring is a valuable means of warning the surgeon of an impending new motor deficit; therefore, other muscle MEPs were also monitored for the functional evaluation. Overall, alterations in most muscle MEPs tended to be in accordance with those of the APB muscle MEPs.

The functionality of the pyramidal tract during surgery was confirmed by intraoperative electrical MEP monitoring so that we could evaluate the relationship between the MEP findings and postoperative motor function. During the removal of the lateral and posterior wall of the tumor (adjacent to the motor cortex), MEPs were carefully monitored in an attempt to prevent them from decreasing in amplitude.

**Statistical Analysis**

All data are represented as means ± SDs. Different groups of patients were compared using the two-tailed Student t-test for independent pairs or a one-way analysis of variance with the Student-Newman-Keuls post hoc analysis (SPSS, Inc., Cary, NC). Differences were considered significant at a probability level equal to or less than 0.05.

**Results**

In all 80 cases the mapping procedure successfully localized the central sulcus and the motor cortex. The somatosensory evoked potential phase reversal alone identified the central sulcus in 77 patients (96.25%). The types and locations of the lesions are summarized in Table 1. Control values of the spinal and muscle MEPs are summarized in Table 2.

Each case was assigned to one of four groups (Tables 3 and 4) according to final changes in the intraoperative MEPs: 1) Group A, in which there was increased amplitude in the muscle MEP with increased I3 wave amplitude (12...
cases); 2) Group B, in which there was no significant change in the MEPs (43 cases); 3) Group C, in which there was decreased muscle MEP amplitude (<35% of the control) with decreased I wave amplitude but an unchanged D wave (15 cases); or 4) Group D, in which the muscle MEP was immediately abolished and the D wave amplitude was decreased (decrease <55% of control value; 10 cases). Deterioration in the latency period, with or without a change in amplitude, was not observed in any case.

In patients in Group A, the increase in the amplitude of muscle MEP was statistically significant as compared with Groups B, C, and D.

<table>
<thead>
<tr>
<th>Group (Type)</th>
<th>D</th>
<th>I1</th>
<th>I2</th>
<th>I3</th>
<th>Muscle MEP</th>
<th>Preop</th>
<th>Postop Day 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>mean</td>
<td>104.16</td>
<td>110.87</td>
<td>114.35</td>
<td>202.43 †</td>
<td>188.75 †</td>
<td>4.91</td>
</tr>
<tr>
<td>B</td>
<td>mean</td>
<td>99.58</td>
<td>98.95</td>
<td>98.99</td>
<td>99.08</td>
<td>97.48</td>
<td>4.97</td>
</tr>
<tr>
<td>C</td>
<td>mean</td>
<td>104.08</td>
<td>82.62 ‡</td>
<td>80.11 ‡</td>
<td>19.99 ‡</td>
<td>21.81</td>
<td>4.93</td>
</tr>
<tr>
<td>D</td>
<td>mean</td>
<td>39.75 §</td>
<td>32.16 ‡</td>
<td>35.51 ‡</td>
<td>20.01 ‡</td>
<td>0</td>
<td>4.91</td>
</tr>
</tbody>
</table>

* Postoperative value/preoperative control value.
† p < 0.05 compared with Groups B, C, and D.
‡ p < 0.05 compared with Group A; p < 0.05 compared with Group B.
§ p < 0.05 compared with Groups A, B, and C.

**TABLE 4**

Postoperative changes in corticospinal and muscle MEPs and motor function in groups

**Fig. 1.** Case 1, Group A. Simultaneous corticospinal and corticomuscular MEP tracings recorded during intracranial surgery showing the response to direct electrical stimulation of the motor cortex in a 68-year-old woman harboring a right frontoparietal meningioma. Definite corticospinal D, I1, and I2 waves could be recorded in this case. The I3 wave could not be recorded at the beginning of the operation (first trace). The corticospinal D wave did not change throughout the entire operative procedure. The transient unstable recording of I waves and the simultaneous abolishment of the muscle MEP on compression of the motor cortex abated immediately after release of compression. After tumor removal, the I3 wave appeared and the muscle MEP increased in amplitude (fourth trace, arrow).
the muscle MEP (range of increase 128–280%, mean increase 188.75 ± 48.79%) correlated with an enhanced increase in the I3 wave in the corticospinal MEPs (range of increase 152.1–260%, mean increase 202.43 ± 43.22% in 12 cases; Fig. 1). Even if the I3 wave did not appear until the end of surgery, there were moderate increases in the I1 or I2 wave (Cases 3 and 4). Most of these patterns were observed in patients harboring meningiomas (10 [83.3%] of 12 cases; Table 3). Postoperative motor performance was not significantly changed in this group. Patients in Group B displayed no changes in muscle or corticospinal MEPs (the mean of all components, corticospinal D and I waves and muscle MEPs, ranged from 97.48 to 99.08% of control values. Motor functions were preserved. Five patients in Group B experienced no transient deficiency syndrome of the SMA associated with tumor resection in that region (partial removal in all cases). Patients in Group C showed a substantial decrease in the amplitude of the muscle MEP (range of decrease 5.3–34.8% of the control waveform, mean change 21.81 ± 10.93%; p < 0.05 compared with Groups A and B) without deterioration in the corticospinal D wave (range 98–118% of the control, mean 104.08 ± 7.31%). Nevertheless, clear suppressions of the I1, I2, and I3 waves at several levels were observed (range of suppression 5.3–95.2%, means 82.62, 80.11, and 19.99%, respectively; p < 0.05 compared with Groups A and B). These patients exhibited severe immediate postoperative motor dysfunction (MMT Scores 0–1), which lasted for several weeks, but gradually recovered to baseline. In Case 58 (Fig. 2), the muscle MEP magnitude fluctuated gradually, decreasing in amplitude until it finally reached 21.5% of the control. The corticospinal D, I1, and I2 waves showed no significant changes, however. At the end of surgery, only the I3 wave had decreased by 11%, but severe motor palsy lasted for 3 weeks. Even after full recovery from motor palsy at 3 months postsurgery, there was still a slight difficulty in fine finger movement. Patients in Group D exhibited a decrease in the corticospinal D wave (range of decrease 21.5–55%, mean decrease 39.75 ± 11.45%; p < 0.05 compared with Groups A, B, and C), which lasted several hours after the immediate abolishment of the muscle MEPs. These patients never recovered from a postoperative severe motor paresis (MMT Scores 0–1). In Case 73, corticospinal D and I waves did not seem to be significantly damaged at the moment the muscle MEP disappeared (Fig. 3 arrow at fourth trace); however, the muscle MEP never recovered and the D wave was suppressed by 32% at the end of the operation (Fig. 3, arrowhead at sixth trace).

The profiles of the corticospinal D, I1, I2, and I3 waves as well as the muscle MEP at the end of surgery (the percentage of the MEP amplitude based on dividing the postoperative amplitude by the preoperative control amplitude) in each group are compared in Table 4 and Fig. 4. The time courses of motor performance scores (MMT scores) in each group are compared in Fig. 5. Changes in the amplitude of the muscle MEP were clearly correlated with I waves both in improvement and deterioration; however, an approximately 50% decrease in D wave amplitude was correlated
with the permanent abolishment of muscle MEP and permanent palsy. A deterioration in the amplitude of the I waves without a change in that of the D wave led to an immediate severe decrease in the muscle MEP amplitude (mean 21.81%) and severe palsy, followed by a gradual improvement.

Discussion

We present our view on a current problem: the interpretation of intraoperative MEP changes. A comparison between intraoperative MEPs recorded from muscles and MEPs recorded from the epidural space in 80 patients with brain tumors resulted in the classification of cases into four different groups according to the final changes in the intraoperative MEPs.

Persistent reductions in intraoperative muscle MEPs that were less than 35% of the control waveform were associated with immediate but transient postoperative motor deficits. An important observation in the present study was that there were two different patterns of corticospinal descending volleys in which patients exhibited severe motor paresis immediately after surgery.

It is widely accepted that a postoperative corticospinal D wave whose amplitude is greater than 50% of the control amplitude leads to the prevention of complete permanent paresis. The present data provide further confirmation of findings of previous studies about the reliability of MEPs with a corticospinal D wave in cases in Group D. The findings of the present study demonstrate that an important clinical limit—less than 35% reduction in the amplitude of the muscle—is relatively safe because if it is not exceeded, it is likely that the patient will recover from any postoperative deficit, whereas a complete loss of MEPs is predictive of a permanent poor outcome. In recent studies in which less invasive intraoperative muscle MEP monitoring

Fig. 3. Case 73, Group D. Simultaneous corticospinal and corticomuscular MEP traces recorded during intracranial surgery in response to direct electrical stimulation of the motor cortex in a 66-year-old man with a right frontal GBM. Corticospinal D, I1, I2, and small I3 waves could be recorded in this case (first trace). The corticospinal D wave decreased by 33.1% during the operative procedure. A decrease in the D wave lasted several hours after complete abolishment of the muscle MEP (fourth trace, arrow) and never recovered. Severe motor paresis persisted in this patient.

Fig. 4. Bar graph showing mean percentages of MEP amplitudes (amplitude at the end of the operation/post./amplitude in the preoperative control site) in the corticospinal D, I1, I2, and I3 waves and the muscle (corticomuscular) MEPs. The cases were assigned to groups (A–D) based on final changes in MEP amplitude and are labeled Types A to D, respectively. See text for definition of groups. *a: p < 0.05 compared with Groups (Types) A, B, and C; *b: p < 0.05 compared with Group (Type) A; *c: p < 0.05 compared with Group (Type) B; *d: p < 0.05 compared with Groups (Types) B, C, and D.
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was performed, researchers found that a spontaneous shift in the latency period (> 15%) and an irreversible sudden reduction in amplitude (> 50–80% of control) together constitute a warning criterion.11,12,14 The degree of postoperative worsening of motor function was correlated with the degree of intraoperative muscle MEP amplitude reduction.14,29 These criteria are compatible with our observations.

It is critically important to assess such a technique’s value and, although not demonstrated in the present study, whether MEP monitoring can improve outcome. It is possible that there is a correlation between changes in spinal and muscle MEPs and eventual motor outcome, but the intraoperative evaluation of these changes might not enable a reduction in morbidity through a modification of surgery. Future studies will be needed to determine the true predictive value of spinal and muscle MEPs.

It is noteworthy that the pattern of alteration in corticospinal descending volleys in a group of patients with moderate muscle MEP deterioration (Group C) was substantially different from that in a group of patients with irreversible muscle MEP abolishment (Group D). Complete and irreversible loss in muscle MEP amplitude can be interpreted as a sign of irreversible damage to the motor system. This can probably be attributed to a lesion of subcortical pyramidal fibers. On the other hand, a moderate progressive deterioration in muscle MEPs (mean reduction 21.81% in final amplitude) was also associated with a decrease in the I3 wave amplitude (Group C). Damage to the cortical gray matter may lead not to axonal but preferentially to interneuronal dysfunction. This damage may include mechanical injury, ischemia, and metabolic failure by compression.

Regardless of the initial causes of the damage, functional cortical interneuronal failure must occur in broad areas of the motor cortex. This functional failure might lead to the failure of the synchronized activation required for I waves in response to electrical stimulation of the motor cortex. Even when the corticospinal tracts are spared, these interneuronal functional failures in motor cortices may cause immediate severe motor paresis. The most likely explanation is that neuronal damage related to motor cortical compression and the manipulation necessary for tumor removal has compromised function in the interneuronal circuitry responsible for I wave generation, leading perhaps to a reduced number and/or dispersion of I waves in the corticospinal tract. Thus, a lack or dispersion of I wave volleys leads to an elevation of the RMT because multiple descending volleys are required to discharge resting spinal motor neurons. This may provide one explanation for the clinical finding that transient motor paresis appeared immediately after surgery and fine voluntary motor function was poor during the chronic phase in these patients. These clinical observations are correlated with the finding in the experimental setting that the D wave survives after removal of gray matter. Therefore, the D wave is thought to originate from stimulation of corticospinal axons in the subcortical white matter. The I waves are abolished by this procedure and are much more sensitive than the D wave to interventions such as cooling and anesthesia. They are thought to be produced by transynaptic activation of the corticospinal neurons in the cortex. On the other hand, it should be noted that an increased resting threshold and a lack of I waves in descending volleys dominated by a D wave are not always

Fig. 5. Graph depicting motor performance scores in patients who underwent surgery for brain tumors. The scores were measured at weekly intervals for 90 days. An analysis of variance showed the scores to be significantly greater in Groups (Types) A and B than in Groups (Types) C and D during the initial 30 days and greater in Groups A, B, and C than in Group D at 90 postoperative days. The individual probability values were less than 0.05 compared with Groups A and B at each time point.
accompanied by poor motor function such as that found in patients with epilepsy or cerebral cortex atrophy during the chronic phase."

Conclusions

In fact, during surgery muscle MEPs are much more sensitive for detection of immediate motor cortical damages than corticospinal MEPs (D wave). Further studies will be required to ascertain the clear functional correlation between corticospinal D and I waves and muscle MEPs and precise motor performance.

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References


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