Sensitivity and specificity in transcranial motor-evoked potential monitoring during neurosurgical operations

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Abstract

Background: Intraoperative transcranial motor-evoked potential (TCMEP) monitoring is widely performed during neurosurgical operations. Sensitivity and specificity in TCMEP during neurosurgical operations were examined according to the type of operation.

Methods: TCMEP monitoring was performed during 283 neurosurgical operations for patients without preoperative motor palsy, including 121 spinal operations, 84 cerebral aneurysmal operations, and 31 brain tumor operations. Transcranial stimulation at 100–600 V was applied by screw electrodes placed in the scalp and electromyographic responses were recorded with surface electrodes placed on the affected muscles. To exclude the effects of muscle relaxants on TCMEP, compound muscle action potential (CMAP) by supramaximal stimulation of the peripheral nerve immediately after transcranial stimulation was used for compensation of TCMEP.

Results: In spinal operations, with an 80% reduction in amplitude as the threshold for motor palsy, the sensitivity and specificity with CMAP compensation were 100% and 96.4%, respectively. In aneurysmal operations, with a 70% reduction in amplitude as the threshold for motor palsy, the sensitivity and specificity with CMAP compensation were 100% and 94.8%, respectively. Compensation by CMAP was especially useful in anurysmal operations. In all neurosurgical operations, with a 70% reduction in amplitude as the threshold for motor palsy, the sensitivity and specificity with CMAP compensation were 95.0% and 90.9%, respectively.

Conclusions: Intraoperative TCMEP monitoring is a significantly reliable method for preventing postoperative motor palsy in both cranial and spinal surgery. A 70% reduction in the compensated amplitude is considered to be a suitable alarm point in all neurological operations.

Key Words: Cerebral aneurysm, compound muscle action potential, motor-evoked potential, spinal operation, transcranial stimulation
INTRODUCTION

In recent neurosurgical operations, newly developed neurological deficits are not considered acceptable as a postoperative complication even in a lifesaving operation. To prevent such deficits, intraoperative neurophysiological monitoring has been widely applied in brain tumor operations, cerebrovascular disease operations, spinal operations, and microvascular decompression.\(^1,7,10,24\) Motor evoked potential (MEP) is used to monitor motor function, and while MEP is more difficult than other evoked potential monitoring, the monitoring of MEP is the most important in neurosurgical operations.\(^2,10\) MEP has become popular due to the recent rapid advances with Propofol anesthesia and the train stimulation method.\(^1,16\)

To record MEP, we must stimulate a primary motor cortex in the frontal lobe or pyramidal tract by one of two methods. The first involves direct stimulation of the motor cortex at around 10 mA using subdural electrodes according to the definition of the primary motor area by somatosensory evoked potential or SEP (cortical MEP or CMEP).\(^8,10,12,24\) The other method involves high-voltage (several hundred volts) transcranial stimulation using screw electrodes that have been placed in the scalp (transcranial MEP or TCMEP).\(^7,14,21,32\)

For different types of operation, which should give an alarm in TCMEP monitoring, we examined the sensitivity and specificity at the alarm point, as well as the reliability and utility of TCMEP monitoring in neurosurgical operations.

MATERIALS AND METHODS

Intraoperative TCMEP monitoring was performed in 342 neurosurgical operations from December 2001 to March 2011. In this report, we analyzed 283 neurosurgical operations with TCMEP compensated by compound muscle action potentials (CMAPs) after peripheral nerve stimulation documented bellow, for the patients without preoperative motor palsy, and accepted paralysis in the operated procedure/the amplitude of MEP before the operative procedure. The relative amplitude index was defined as the amplitude of MEP after the relative amplitude index and relative amplitude index compensated by the amplitude of CMAP were calculated automatically with Microsoft Excel on an MEB personal computer.

Postoperative motor function was judged at 1 week after operation. Our definition of motor palsy was less than 2/5 of the muscle strength by MMT at 1 week after the operation. False-negative results were diagnosed as motor palsy less than 2/5 of the muscle strength by MMT continuing more than a week without significant MEP amplitude decrease. False-positive results were diagnosed as motor function more than 2/5 of the muscle strength by MMT at a week after the operation with significant MEP amplitude decrease. Of course, motor function immediately after the operation had been certainly observed, but it was not statistically analyzed. Long-term outcome, exactly permanent motor function, was also not analyzed in our series.

For the analysis, we referred to a report by Langeloo et al. that an 80% reduction in amplitude was significant in spinal surgery.\(^11\) The relative amplitude indexes with and without CMAP compensation were calculated at the beginning of the operative procedure (at the introduction of the microscope after craniotomy in a cranial operation) and at the end of the procedure (just before dural closure in a cranial operation).\(^29\) The alarm-
point amplitude reduction rate of postoperative motor palsy was determined according to the sensitivity and specificity of each amplitude reduction. Finally, statistical analyses were performed using Fisher’s exact probability test to verify that our TCMEP could detect postoperative motor palsy. These analyses were performed in cerebral aneurysmal operations, spinal operations, brain tumor operations, and all neurosurgical operations. The efficacy of compensation by CMAP after peripheral nerve stimulation was also examined.

RESULTS

Overall, no adverse events were noted with high-voltage transcranial stimulations or electromyogram recordings. TCMEP could be recorded in all 283 operations. In cranial operations, TCMEP was performed immediately after artificial cerebrospinal fluid (CSF) infiltrated the operative field, since the amplitude had been reduced after CSF removal. Temporary amplitude reduction was also observed in patients with little cerebral cross-flow during temporary internal carotid artery occlusion in CEA or the use of a temporary clip in aneurysmal operations. Arterial stenosis due to clipping of the aneurysm and long-term cerebral compression by a retractor induced a reduction in the amplitude of TCMEP. In these cases, the amplitude was soon recovered by recanalization of the artery or a pause in the operative procedure. In spinal operations, a temporary disappearance or severe reduction in the amplitude of TCMEP immediately after decompression was observed in two lumbar spinal canal stenosis operations and two cervical spondylosis operations.

Sensitivity, specificity, and setting of the alarm point in transcranial motor-evoked potential

For each type of operation, sensitivities and specificities were calculated according to the amplitude reduction rate (30–100%, every 10%) with or without compensation by CMAP after peripheral nerve stimulation in 283 patients without preoperative motor palsy under MMT 3/5 [Table 1]. In spinal operations, since the sensitivity was 100% and the specificity was greater than 95% with or without CMAP compensation, the threshold amplitude reduction rate for postoperative motor palsy was taken to be 80%. On the other hand, in aneurysmal operations, since the sensitivity and specificity were 100% with CMAP compensation and 94.8%, respectively, in this case the threshold should be set at 70% amplitude reduction. Without CMAP compensation, the sensitivity at a 70% reduction in amplitude was less than 90%. In brain tumor operations, the maximum sensitivity was 75% even with CMAP compensation. In all neurosurgical operations, the threshold of postoperative motor palsy in TCMEP should be 70% amplitude reduction because the sensitivity was the highest at 70% amplitude reduction.

| Amplitude reduction | Spinal operation (N = 121) | Aneurismal operation (N = 84) | Brain tumor operation (N = 31) | All neurosurgical operation (N = 283) |
|---------------------|---------------------------|-----------------------------|-------------------------------|-------------------------------------|
| CMAP compensation (-) | Sensitivity | Specificity | Sensitivity | Specificity | Sensitivity | Specificity | Sensitivity | Specificity |
| 30                  | 100.0         | 95.0          | 75.0            | 83.1          | 97.4            | 95.0          | 90.0            | 85.0          |
| 50                  | 100.0         | 95.0          | 83.1            | 95.0          | 97.4            | 95.0          | 90.0            | 85.0          |
| 60                  | 100.0         | 95.0          | 83.1            | 95.0          | 97.4            | 95.0          | 90.0            | 85.0          |
| 70                  | 100.0         | 95.0          | 83.1            | 95.0          | 97.4            | 95.0          | 90.0            | 85.0          |
| 80                  | 100.0         | 95.0          | 83.1            | 95.0          | 97.4            | 95.0          | 90.0            | 85.0          |
| 90                  | 100.0         | 95.0          | 83.1            | 95.0          | 97.4            | 95.0          | 90.0            | 85.0          |
| 100                 | 100.0         | 95.0          | 83.1            | 95.0          | 97.4            | 95.0          | 90.0            | 85.0          |

CMAP: Compound muscle action potentials, Figures in parentheses are in percentage.
Statistical analysis of intraoperative transcranial motor-evoked potential monitoring

Fisher’s exact probability test was performed based on 2 × 2 tables of the results of 283 instances of TCMEP monitoring in patients without preoperative motor palsy (MMT < 3/5) according to the presence or absence of postoperative motor palsy, and the presence or absence of significant amplitude reduction (spinal and brain tumor, >80%; aneurysm and all, >70%) [Table 2]. All the test results showed statistically significant differences \( P < 0.05 \), and thus TCMEP monitoring could detect newly developed postoperative motor palsy.

Case 1

A 58-year-old woman was admitted with Wallenberg syndrome due to occlusion of the right posterior inferior cerebellar artery [Figure 1a]. Her angiogram showed a basilar bifurcation aneurysm [Figure 1b, c]. Two months after the infarction, a craniotomy was performed. Neck clipping of the aneurysm was through a right anterior temporal route. Her TCMEP with 300 V stimulation of the left APB and bilateral abductor hallucis (AH) muscles disappeared with temporary occlusion of the basilar artery for 10 min [Figure 1d, arrow] and partially recovered by recirculation after neck clipping [Figure 1d, arrow head]. An 81% reduction in amplitude was observed in the left AH muscle by CMAP after peripheral nerve stimulation compensation. Postoperatively, monoparesis appeared in her left lower limb and persisted for a month. Angiography after the operation showed complete neck occlusion [Figure 1e, f]. This was a true-positive case.

Case 2

A 47-year-old man had been struck by a motor vehicle while on his bicycle and suffered from motor weakness of his hands. The magnetic resonance image of his cervical spine showed marked spinal canal stenosis at C3-6 by spondylotic change [Figure 2a–c]. Right C3-6 unilateral open-door laminoplasty with titanium miniscrews and miniplates through hydroxyapatite ceramic spacers was performed a month after the trauma [Figure 2d]. Although full decompression was achieved [Figure 2e] and bilateral grasping force was recovered postoperatively, the amplitudes of TCMEP on the bilateral APB muscles decreased after decompression. The final amplitude reduction rates were 96% (left APB) and 89% (right APB) with CMAP compensation. This was a false-positive case.

DISCUSSION

Prior to the introduction of Propofol anesthesia, intraoperative monitoring by SEP had been used in neurosurgery.\[22\] SEP is easily obtained by placing electrodes on the scalp and is less susceptible to

| Spine | Brain tumor |
|-------|-------------|
| Monitoring outcome | CMAP compensation (−) | Clinical outcome | CMAP compensation (−) | Clinical outcome |
| 80% or more decrease of amplitude | + | true positive | 9 | false negative | 1 | Positive predictive rate 64% |
| 60% or more decrease of amplitude | − | false negative | 0 | true negative | 4 | Negative predictive rate 100% |
| \( P < 0.00001 \) (Fisher’s test) | Sensitivity 95.6% | Specificity 96.4% | | |

| Aneurysm | All operations |
|---------|--------------|
| Monitoring outcome | CMAP compensation (−) | Clinical outcome | CMAP compensation (−) | Clinical outcome |
| 70% or more decrease of amplitude | + | true positive | 6 | false positive | 0 | Positive predictive rate 67% |
| 70% or more decrease of amplitude | − | false negative | 0 | true negative | 3 | Negative predictive rate 100% |
| \( P < 0.00001 \) (Fisher’s test) | Sensitivity 95.7% | Specificity 96.1% | | |

Table 2: 2 × 2 tables of the results of 283 instances of TCMEP monitoring in patients without preoperative motor palsy according to the presence or absence of postoperative motor palsy, and the presence or absence of significant amplitude reduction (spinal and brain tumor, >80%; aneurysm and other, >70%)
Figure 1: Case 1. A 58-year-old woman was admitted with Wallenberg syndrome due to occlusion of the right posterior inferior cerebellar artery (a). Her angiogram showed a basilar bifurcation aneurysm (b, c). Two months after the infarction, a craniotomy for neck clipping was performed. Her transcranial motor-evoked potential with 300-V stimulation disappeared with temporary occlusion of the basilar artery for 10 min (d, arrow) and partially recovered by recirculation after neck clipping (d, arrow head). Postoperatively, angiography after the operation showed complete neck occlusion (e, f).

Figure 2: Case 2. A 47-year-old man had been struck by a motor vehicle while on his bicycle and suffered from motor weakness of his hands. The magnetic resonance image of his cervical spine showed marked spinal canal stenosis at C3-6 by spondylotic change (a–c). Right C3-6 unilateral open-door laminoplasty was performed a month after the trauma (d). Although full decompression was achieved (e), the amplitudes of transcranial motor-evoked potential decreased after decompression. The final amplitude reduction rates were 96% (left abductor pollicis brevis) and 89% (right abductor pollicis brevis) with compound muscle action potential compensation.
anesthesia, but cannot detect changes in motor function. Since the introduction of Propofol anesthesia, MEP monitoring has become more widespread.\[^{1}\] In brain surgery, MEP has been reported to be more sensitive than SEP for detecting motor disturbance by cerebral ischemia.\[^{6,12,18,25,26,28}\]

As noted previously, there are two ways to stimulate the motor cortex: direct cortical stimulation and transcranial stimulation. On the other hand, direct (D) waves can be obtained from epidural electrodes in the cerebral spine as spinal cord-evoked potentials rather than being obtained with surface or needle electrodes as is usually done with EMG.\[^{18}\] By combining different modes of stimulation and derivation, we can determine MEP in four ways. As been described by Deletis et al. and Fujiki et al., the underlying conductivity of the corticospinal tract can only be partially deducted from the recorded MEPs.\[^{14,16}\] Although it is possible to obtain stable readings from an epidural electrode on the cerebral spine by addition, addition takes time, and even under general anesthesia, electrode insertion is somewhat dangerous. EMG derivation is convenient, but slightly less stable, and therefore we use CMAP compensation through peripheral nerve stimulation.\[^{28}\] Fujiki et al. mentioned that during surgery, monitoring of corticomuscular MEPs [which are related to indirect (I) waves] is a much more sensitive method for the detection of immediate motor cortical damage than monitoring of corticospinal MEPs (D wave).\[^{16}\]

MEP by direct motor area stimulation is highly sensitive and is widely used not only in operations for brain tumors adjacent to a motor area or pyramidal tract, but also in cerebrovascular operations, such as clipping of an aneurysm.\[^{22,24}\] Direct motor area stimulation that seems to be more reliable than TCMEP should be performed in craniotomy. However, cortical mapping of the motor area, which is usually performed by cortical SEP, is not very convenient, and may take a long time. The insertion of electrodes for direct CMSEP is sometimes difficult because of the high intracranial pressure after subarachnoid hemorrhage, and because of adhesion as a re-operation. Direct MEP is more susceptible to anesthetics, and monitoring cannot be performed if the electrode for direct MEP moves.\[^{8}\] Usually, direct MEP with EMG recording can monitor only contralateral APB muscles. In contrast, TCMEP is easy and safe under total anesthesia, and is widely used in spinal surgery.\[^{11,14,21}\] TCMEP makes it possible to monitor the bilateral or upper and lower limbs simultaneously, and seems to be especially useful in operations for anterior communicating artery aneurysm that may cause lower limb dominant or bilateral motor palsy.\[^{28}\] We usually use TCMEP alone in an aneurysmal operation, and in brain tumor surgery we use direct CMEP along with TCMEP as a supporting method.\[^{19,26,32}\]

We use CMAP after peripheral nerve stimulation for the compensation of MEP amplitude change only by muscle relaxants, not by anesthetics.\[^{29}\] Surely, the comparison of the CMAP throughout the surgical procedure will provide information about the muscle end plate, but nevertheless, anesthesia affecting, for example, the excitation of the alpha-motor neuron might result in an MEP decrement not being surgically related. This may only be detected by comparing MEPs of the healthy and the affected side. Indeed, comparing MEPs of the other, healthy side can compensate the effect of anesthetics on the excitation of the alpha-motor neuron. In the thoracic-lumbar spinal operation, comparing MEPs of the upper extremity and the lower extremity seemed to be useful. CMAP after peripheral nerve stimulation can constantly compensate the effect of muscle relaxants in all neurosurgical operations.

In TCMEP, the stimulated site, body movement due to high-voltage stimulation, and the difficulty of judging changes in amplitude and latency have been reported to be controversial. The stimulated site has been reported to be the brain stem as calculated by the latency after extreme high-voltage (960 V) transcranial stimulation.\[^{30}\] In the recent times, 5-pulse train stimulation has been commonly used for MEP. With an inter-pulse interval of 2 msec, a 5-pulse train of 0.2 msec stimulation requires 9 msec. Since it is unclear when the actual ignition occurs during this 9 msec, it is impossible to estimate the true latency and then identify the stimulated site in TCMEP. We previously reported that transcranial stimulation at a lower voltage led to ignition closer to a motor area, as low-voltage transcranial stimulation induced EMG recording only on the side contralateral to the anode, and the wave form and latency were similar to those after direct cortical stimulation.\[^{27}\] Rothwell also suggested that if the voltage of TCMEP was reduced to near the threshold level, the area near the motor area was stimulated.\[^{21}\] Body movement due to stimulation was also considerably reduced by a reduction in the stimulation voltage from the commonly used 600 V to 300–400 V. In some institutes, TCMEP can be recorded with 100–200 V stimulation because of advances in anesthesia and monitoring. However, it is reasonable to consider that the amplitude of EMG should be evaluated under supramaximum stimulation.\[^{15}\] TCMEP using stimulation with too low voltage cannot be reliable. We usually begin TCMEP from 500-V stimulation.

The statistically significant changes in TCMEP amplitudes were consistent with the clinical outcomes in patients without preoperative motor palsy, and this clarified the clinical usefulness of TCMEP. With regard to the stimulated site of TCMEP, it is well known that temporary occlusion of the internal carotid artery or middle cerebral artery causes a reduction in the amplitude of TCMEP.\[^{7,28}\] These clinical findings suggest that the simulated site of TCMEP is not the brain stem,
and is at least above the posterior limb of the internal capsule. Since the stimulated site seems to be able to change after craniotomy and the removal of CSF, this problem should be investigated in the future.

The sensitivity and specificity of TCMEP vary according to the operation site because the stimulating site of transcranial stimulation is obvious. Alarm point should be set individually according to the operative site. Indeed, the transcranial stimulation might lead to preserve MEPs being caused by deep white matter stimulation, but it is not so important in spinal surgery. It is well known that in spine surgery, amplitude decrement does not result in permanent motor deficit and often results in transient motor deficits. As previously mentioned, postoperative motor palsy was defined a continuous motor palsy with MMT less than 2/5 between the awake from anesthesia and 1 week after the operation. We think that MEP decrement is the result of a very transient motor deficit, but it is recovered until the awake from anesthesia. Transcranial MEP is so sensitive in spinal surgery that subclinical transient motor deficit can be detected. It is also well known that acute decompression causes hyperemia in spinal cord, and it is a major reason for pseudopositives in spinal surgery. Deep white matter stimulation by transcranial stimulation seem to be one of the reasons why false negatives have happened more in those patients undergoing brain surgeries than in those undergoing spinal surgeries.

There is little consensus regarding the evaluation of the amplitude change and alarm point in TCMEP. In direct CMEP recording with cervical epidural electrodes, a 50% reduction in amplitude of the D-wave generally seems to be significant. Kombos et al. reported that an 80% reduction in amplitude was the threshold of postoperative motor palsy in direct CMEP with EMG recording. Langelo et al. also showed that an 80% reduction in amplitude was the alarm point on TCMEP-EMG recording in spinal surgery. We also reported that an 80% reduction in amplitude was the threshold of irreversible motor palsy on TCMEP compensated by peripheral nerve-stimulated CMAP. In the present study, based on this 80% amplitude reduction, intraoperative changes in amplitude on TCMEP were investigated retrospectively. In all the neurosurgical operations, the sensitivity and specificity of TCMEP compensated by peripheral nerve-stimulated CMAP were 83.3% and 98.3%, respectively, if the threshold was defined to be an 80% amplitude reduction. These results are consistent with those of Kombos and Langelo. We use CMAP after peripheral nerve stimulation for the compensation of MEP amplitude change by muscle relaxants, not by anesthetics, and some improvements in sensitivity and specificity were observed with compensation by CMAP after peripheral nerve stimulation. Nevertheless, with regard to the significance of the alarm point, irreversible motor palsy has already occurred at an 80% amplitude reduction. A false-negative result that influences sensitivity is clinically more important than a false-positive result that influences specificity. Thus, it is more important to decrease false negatives in intraoperative monitoring. Accordingly, a 70% relative amplitude should be the alarm point since the highest sensitivity was calculated at 70% reduction in amplitude in all the neurological surgeries. The limit of tumor removal and temporary occlusion of blood flow should be at a 70% amplitude reduction in TCMEP.

In our study, the specificity of TCMEP was 100% in brain tumor and aneurysmal operations, and the sensitivity was 100% in spinal surgery. The relatively low sensitivity of TCMEP in craniotomy seems to be caused by the stimulated site of TCMEP. Conversely, the specificity of TCMEP was relatively low in spinal surgery; TCMEP was too sensitive in spinal surgery. In actual practice, aggressive decompression of the spinal cord or root in laminoplasty often causes a sudden decrease in the amplitude of TCMEP probably due to reversible hyperemia. In these cases, if postoperative motor palsy did not occur, reversible dysfunction of the spinal cord or root may have already recovered immediately after the operation.

In conclusion, the present results show that TCMEP monitoring could predict postoperative motor palsy not only in spinal operations but also in craniotomy. The sensitivity and specificity of TCMEP were improved by compensation with CMAP after peripheral nerve stimulation. Since motor palsy newly develops postoperatively at an 80% reduction in amplitude in TCMEP for patients who do not have preoperative motor palsy, a 70% reduction in amplitude should be considered to be the alarm point of TCMEP.

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