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SURGERY

Evaluation of a Combination of Waveform Amplitude and Peak Latency in Intraoperative Spinal Cord Monitoring

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Study Design. Retrospective study.

Objective. The goal of the study was to investigate the significance of a change in latency in monitoring of transcranial muscle-action potential (Tc-MsEP) waveforms.

Summary of Background Data. Tc-MsEP has become a common approach in spine surgery due to its sensitivity and importance in motor function. Many reports have defined the alarm point of Tc-MsEP waveform as a particular decrease in amplitude, but evaluation of the waveform latency has not attracted as much attention.

Methods. The subjects were 70 patients who underwent spine surgery using intraoperative Tc-MsEP monitoring. The peak latency was defined as the period from stimulation until the waveform amplitude reached its peak. Relationships with post-operative paralysis were examined separately for latency delays of 5% or more and 10% or more, and in combination with a decrease in amplitude of 70% or more from baseline.

Results. Acceptable baseline Tc-MsEP responses were obtained from 1225 of 1372 muscles in the extremities (89.3%). Seven of the 70 patients (10%) had postoperative paralysis. A decrease in intraoperative amplitude of 70% or more from baseline occurred in 25 cases, with sensitivity 100%, specificity 71%, false positive rate 29%, and positive predictive value (PPV) 28% for prediction of postoperative paralysis. Compared to baseline, 15 cases had a latency delay of 5% or more, which gave a sensitivity of 100%, specificity of 87%, false positive rate of 0%, and PPV 47%, and 8 cases had a delay of 10% or more, which gave a sensitivity of 86%, specificity of 97%, false positive rate of 3%, and PPV 75%. A combination of a decrease in amplitude of 70% or more from baseline and a delay in latency of 10% or more from baseline had a sensitivity of 86%, specificity of 98%, and a false positive rate of 2%, and PPV 86%.

Conclusion. Combined use of latency and amplitude could lead to reduction of false positives and increase of PPV in Br(E)-MsEP monitoring.

Key words: Br(E)-MsEP, intraoperative monitoring, latency, latency delay, spine surgery.

Level of Evidence: 3

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The importance of intraoperative spinal cord monitoring for prevention of postoperative paralysis is widely understood.[1–8] Transcranial muscle-action potential (Tc-MsEP) waveforms, brain-stimulated spinal cord–evoked potentials (D-waves), and somatosensory-evoked potentials (SSEPs) have been used for this purpose.[4,7,8] In particular, Tc-MsEPs are widely used for intraoperative spinal cord monitoring, and this has become a common approach due to its increased sensitivity and importance for motor function.[2,5,6] There are previous reports on alarm points for Tc-MsEP based on a decrease in waveform amplitude, but evaluation of the waveform latency has attracted less attention. In this study, we examined the characteristics of latency in Tc-MsEP monitoring.

MATERIALS AND METHODS

Subjects

The subjects were 70 patients who underwent spine surgery using intraoperative Tc-MsEP monitoring at our institution, with 1372 muscles in the extremities chosen for monitoring. The patients had a mean age of 43 years (range, 10–72), and 41 were women and 29 were men. Diseases included intradural extramedullary tumor (n = 26), adolescent idiopathic

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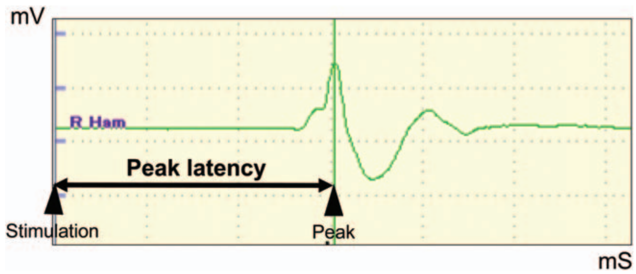


Figure 1. Peak latency was defined as the period from stimulation until the waveform amplitude reached its peak.

scoliosis (n = 16), ossification of posterior longitudinal ligament/ossification of the ligamentum flavum (n = 9), spinal intramedullary tumor (n = 11), congenital scoliosis (n = 3), and others (n = 5). The peak latency was defined as the period from stimulation until the waveform amplitude reached its peak (Figure 1). The percentage latency delay was defined based on comparison with the peak latency at baseline: [(latency-latency at baseline)/latency at baseline] × 100. A decrease in the postoperative manual muscle test (MMT) score of 1 or more compared with the preoperative MMT was defined as postoperative paralysis. Relationships with postoperative paralysis were examined separately for latency delays of 5% or more and 10% or more,[4,9,10] and in combination with a decrease in amplitude of 70% or more from baseline.[3,6] This study was approved by our institutional review board (No. 354-3) and each patient provided informed consent before enrollment.

Anesthetic Management and General Conditions During Surgery

A minimal benzodiazepine dose was used as preanesthetic medication to avoid possible suppression of waveform latency and amplitude. Propofol (3–4 mg/kg), fentanyl (2 mg/kg), and vecuronium (0.12–0.16 mg/kg) were administered for induction, and anesthesia was maintained with propofol (50–100 μg/kg/min), fentanyl (1–2.5 μg/kg/h), and vecuronium (0.01–0.04 mg/kg/h). Concomitant hypotensive anesthesia was given as appropriate with continuous PGE1 and a short-acting β1 blocker (landiolol). Patients were maintained in a normothermic state and the temperature was raised in the event of possible intraoperative spinal damage.[4,11] End-tidal CO_2 was maintained in the reference range throughout surgery. For intraoperative body temperature monitoring, a catheter with a vesical temperature sensor was used. Hemodynamic data were electronically recorded with invasive arterial BP monitoring. Systolic blood pressure variation was measured during surgery and was determined at the time of waveform deterioration.

Stimulation and Recording Methods

A MS120B instrument (Nihon Kohden, Tokyo, Japan) was used to perform transcranial stimulation, using parameters of five stimuli in a row at 2-ms intervals, a constant biphasic current of 200 mA for 500 μs, a 50 to 1000 Hz filter, and a 100-ms epoch time with 20 or more recorded signal responses. The stimulated point was 2 cm anterior and 6 cm lateral from the Cz location over the cerebral cortex motor area. Using the Neuromaster MEE-1232 ver. 05.10 (Nihon Kohden, Japan), which is expandable to 32 channels, muscle action potentials were recorded from the upper and lower extremities *via* a pair of needle electrodes 3 to 5 Tc-MsEPs apart. In cervical spine surgery, the bilateral deltoid, biceps, triceps, brachioradialis, extensor carpi ulnaris, abductor digiti minimi, adductor longus, quadriceps femoris, hamstrings, tibialis anterior, gastrocnemius, abductor hallucis, and anal sphincter muscles were used as target muscles. In thoracic spine surgery, the bilateral deltoid, extensor carpi ulnaris, adductor longus, quadriceps femoris, hamstrings, tibialis anterior, gastrocnemius, abductor hallucis, and anal sphincter muscles were used as target muscles. Tc-MsEP data from these muscles were used for analysis. Multimodal monitoring was used in all cases, with a particular combination of D-waves and SSEPs. The stimulation conditions, including Tc-MsEP, brain-stimulated spinal cord–evoked potentials, and SSEP, are summarized in Table 1. Free running Electromyographys from all the above muscles were also monitored throughout the operation. When Tc-MsEPs from multiple muscles were lost, regardless of the D-wave or SEP status, the neurological situation was considered urgent, and we decided whether or not to continue surgery. A decrease in D-wave amplitude of 50% or more was also considered urgent.

TABLE 1. Monitoring Conditions for Stimulation and Recording

Method	Stimulation/Stimulus	ISI (ms)	Intensity (mA)	Duration (ms)	Recording	Electrodes	Filter (kHz)
Tc-MsEP	Scalp/repeated train of five stimuli	2	200	0.5	Muscles of interest synchronous	Two-needle electrodes/ muscle	0.05–1
Br-SCEP (D-wave)	Scalp/repeated single stimulus	–	200	0.5	Spinal cord epidural or subarachnoid	Bipolar spinal electrode	0.5–3
SSEP	Nerve/repeated single stimulus	–	10	0.2	Scalp	Cz-Fz	10

Br-SCEP indicates brain-stimulated spinal cord evoked potentials; ISI, interstimulus interval; SSEP, somatosensory-evoked potentials;, Tc-MsEP, transcranial muscle-action potential.

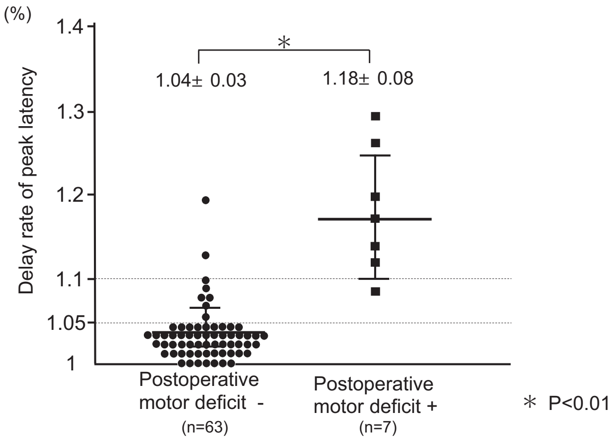


Figure 2. Delay rates of peak latency compared to the control waveform in cases with and without postoperative motor deficit. There was a significant difference between the two groups ($P < 0.01$).

Monitoring and Alert Parameters

The Tc-MsEP baseline was taken immediately after documented surgical exposure of the spine. Waiting until this point for baseline measurements reduced the effects on Tc-MsEP responses because of body and spinal cord temperature changes occurring with exposure. Signals were rechecked after surgical exposure, screw insertion, decompression, and wound closure. Surgeons were informed of an acute change in the Tc-MsEP response. If a waveform changed during surgery, systolic blood pressure was raised or hypotensive anesthesia was reversed, the patient was warmed, and irrigation was performed with warm saline.[4,11] If the waveform did not recover, surgery at the current site was suspended. Surgery at a different site continued until the waveform recovered. If there was no improvement, surgery was terminated.

Statistical Analysis

Significance was assessed by Student t test or Fisher exact test at $P < 0.05$. Data analysis was performed with SPSS ver. 22 for Windows (IBM, Chicago, IL).

RESULTS

Acceptable baseline Tc-MsEP responses were obtained from 1225 of 1372 muscles in the extremities (89.3%) in 70 patients, and 7 of these patients (10%) had postoperative paralysis. The average number of muscles with waveform deterioration was significantly higher in the 7 patients with postoperative paralysis than in the 18 patients without this paralysis (6.7 ± 2.1 *vs.* 2.6 ± 1.1, $P < 0.01$). The peak latency compared to the control waveform differed significantly in cases with and without a postoperative motor deficit ($1.04\% \pm 0.03\%$ *vs.* $1.18\% \pm 0.08\%$, $P < 0.01$) (Figure 2). A decrease in intraoperative amplitude of 70% or more from the Tc-MsEP baseline occurred in 25 cases, with sensitivity 100%, specificity 71%, false positive rate (FPR) 29%, false negative rate (FNR) 0%, positive predictive value (PPV) 28%, and negative predictive value (NPV) 100% for prediction of postoperative paralysis (Table 2). Fifteen cases had a latency delay of 5% or more, giving sensitivity 100%, specificity 87%, FPR 0%, FNR 13%, PPV 47%, and NPV 100% (Table 3). Eight cases had a delay of 10% or more, giving sensitivity 86%, specificity 97%, FPR 3%, FNR 14%, PPV 75%, and NPV 97% (Table 3).

The results for a combination of amplitude and latency are shown in Table 4. Among the 25 cases with a decrease in amplitude 70% or more, latency delays of 5% or more, and 10% or more occurred in 14 (56%) and 7 (28%) cases, respectively. A decrease in amplitude of 70% or more and a delay in latency of 5% or more from baseline had sensitivity 100%, specificity 89%, FPR 11%, and PPV 50% for prediction of postoperative paralysis in the 14 evaluable cases. A decrease in amplitude of 70% or more and a delay in latency of 10% or more from baseline had sensitivity 86%, specificity 98%, FPR 2%, and PPV 86% for prediction of postoperative paralysis in the seven evaluable cases (Table 4).

Illustrative Cases

Case 1: The patient was a 52-year-old man with cervical ossification of posterior longitudinal ligament presenting with bilateral arm paresthesia and clumsiness in walking, but without motor deficit. Following posterior fusion using cervical screws (C4–6), posterior laminectomy was performed (Figure 3A–D). In intraoperative Tc-MsEP monitoring, there was no obvious waveform deterioration in the upper extremities (Figure 4A). The peak latency for the left tibialis anterior muscle during screw insertion was delayed to 42 ms (control 35 ms), giving a delay of 20%; however,

TABLE 2. Relationship of Postoperative Paralysis With Waveform Amplitude Deterioration of 70% More From Baseline

		Postoperative Paralysis		Total
		Present	Absent	
Decrease in amplitude ≥70%	(+)	7	18	25
	(−)	0	45	45
Total		7	63	70

In case of decrease in amplitude of 70% or more, sensitivity was 100%, specificity was 71%, false positive rate was 29%, false negative rate was 0%, positive predictive value was 28%, and negative predictive value was 100%.

TABLE 3. Relationship of Postoperative Paralysis With Waveform Latency Delay 5% or More and 10% or More From Baseline

		Postoperative Paralysis		Total
		Present	Absent	
Latency delay ≥5%	(+)	7	8	15
	(−)	0	55	55
Total		7	63	70
Latency delay ≥10%	(+)	6	2	8
	(−)	1	61	62
Total		7	63	70

In case of latency delay 5% or more, sensitivity was 100%, specificity was 87%, false positive rate was 0%, false negative rate was 13%, positive predictive value was 47%, and negative predictive value was 100%.

In case of Latency delay ≥10%, sensitivity was 86%, specificity was 97%, false positive rate was 3%, false negative rate was 14%, positive predictive value was 75%, and negative predictive value was 97%.

TABLE 4. Evaluation Using a Combination of Amplitude and Latency

Condition	Sensitivity (%)	Specificity (%)	False Positive Rate (%)	PPV (%)
Decrease in amplitude of ≥70% from baseline	100	71	29	28
Delay in latency of ≥5% from baseline	100	87	13	47
Decrease in amplitude of ≥70% + delay in latency of ≥5% from baseline	100	89	11	50
Delay in latency of ≥10% from baseline	86	97	3	75
Decrease in amplitude of ≥70% + delay in latency of ≥10% from baseline	86	98	2	86

PPV indicates positive predictive value.

no muscles had waveforms in which amplitude decreased by 70% or more. There was also no obvious change in the waveform at the end of surgery (Figure 4B). Postoperatively, clumsiness in walking improved, and MMT score and neurological function did not worsen.

Case 2: A 54-year-old woman underwent surgery for numbness of the upper limbs and gait disturbance due to a cervical intramedullary tumor. T2-weighted and gadolinium-enhanced magnetic resonance imaging revealed severe canal stenosis due to a tumor at C4–6 (Figure 5A–C). In intraoperative Tc-MsEP monitoring, there was no waveform deterioration in the upper extremities (Figure 6A). The peak latency for the left gastrocnemius muscle during tumor resection was delayed to 39 ms (control 33 ms), giving a delay of 18%, and the bilateral abductor hallucis, quadriceps femoris, anal sphincter, and right hamstrings and

Figure 3. The patient was a 52-year-old man with cervical ossification of posterior longitudinal ligament (OPLL) presenting with cervical spondylotic myelopathy shown in (**A**) sagittal CT and (**B**) sagittal T2-weighted magnetic resonance imaging (MRI). (**C, D**) Posterior laminectomy with fusion using pedicle screws (C4–6) was performed.

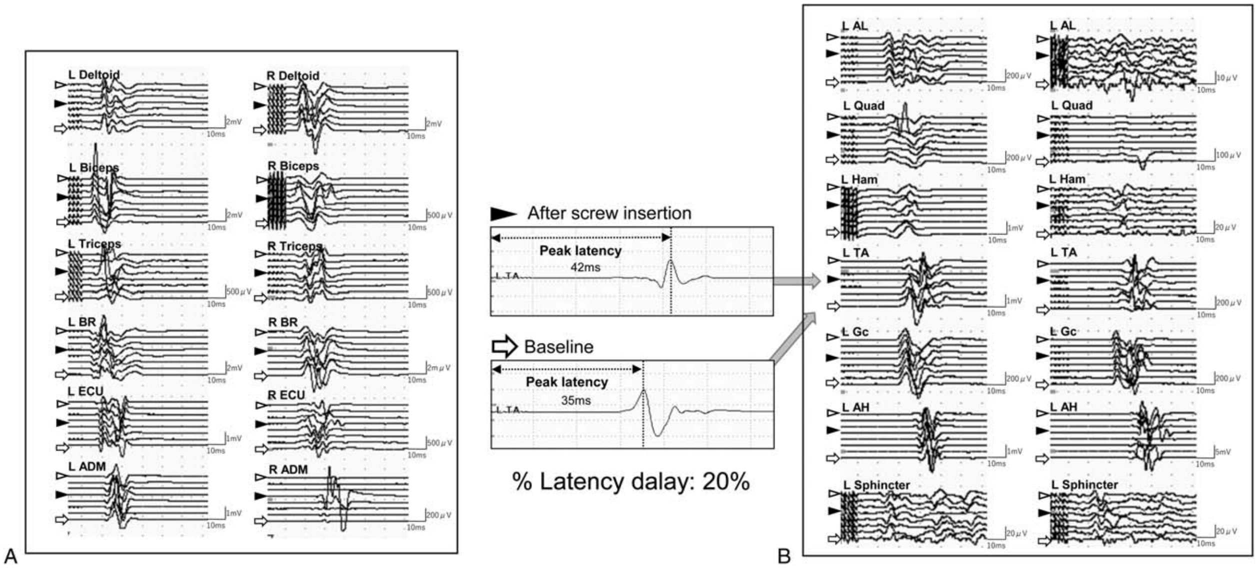


Figure 4. Intraoperative Tc-MsEP monitoring. **A**, There was no obvious waveform deterioration of the upper extremity. **B**, Compared with baseline (open arrow), the peak latency for the left tibialis anterior during screw insertion was delayed to 42 ms (control 35 ms), giving a delay of 20% (arrowhead); however, regarding amplitude, there were no muscles in which all waveforms decreased by 70% or more and there was no deterioration at the end of surgery (open arrowhead). After surgery, the manual muscle test (MMT) score and neurological function did not worsen.

gastrocnemius showed an amplitude decrease of 70% or more from baseline. There was no clear recovery of the waveforms at the end of surgery (Figure 6B). Postoperatively, the pathological diagnosis was meningioma. The strength of the lower limb proximal muscle decreased from a preoperative MMT of 5 to a postoperative MMT of 4, and numbness of upper limbs continued for 3 months.

DISCUSSION

Intraoperative Tc-MsEP alarm points have previously focused mainly on waveform amplitude.[1–3,6,11–16] As alarm point criteria, for intramedullary spinal cord tumor, Quiñones-Hinojosa *et al*[1] used the multiphase of the waveform, Sala *et al*[12] used waveform amplitude disappearance and a 50% or more D-wave amplitude decrement. For spinal deformity surgery, Langeloo *et al*[2] used a decrease in amplitude of 80% or more from the Tc-MsEP baseline. And, for overall spinal surgery, Ito *et al*[3] and Kobayashi *et al*[6] proposed a decrease in amplitude of 70% or more from the Tc-MsEP baseline. In Tc-MsEP monitoring at the amplitude alarm point, sensitivity is reported to be 100%, but the FPR is also high.

The latency of the waveform has been examined as the electrophysiological latency in animal models. Zencirci *et al*[17] showed that the latency was delayed in a rat sciatic nerve injury model and shortened after treatment, and Eitan *et al*[18] reported that latency values were delayed compared with normal values in regeneration of central nervous system axons in a rat optic nerve injury model. However, there are few clinical reports of latency and no study has examined alarm points using a combination of amplitude and latency.

In our series, a criterion of an amplitude of 70% or more from baseline gave a sensitivity of 100%, but the FPR was 29%, and PPV was 28%. Using a latency delay of 10% or more from baseline, the sensitivity was 100%, the FPR was only 3%, and PPV was 75%. A combination of a decrease in amplitude of 70% or more from baseline and a latency delay of 10% or more from baseline in two applicable cases gave

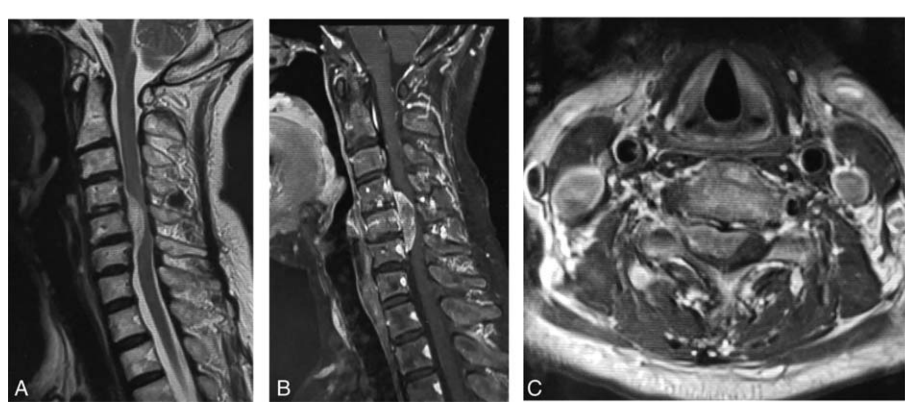
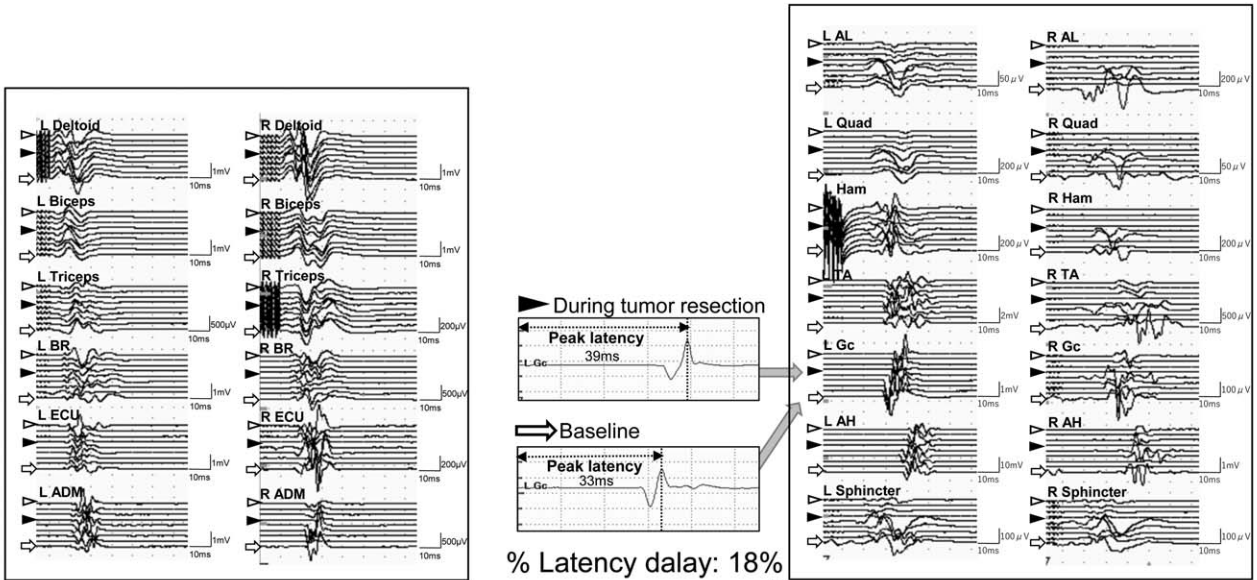


Figure 5. A 54-year-old woman underwent surgery for numbness of the upper limbs and gait disturbance due to a cervical intramedullary tumor found in (**A**) sagittal T2-weighted magnetic resonance imaging (MRI), (**B**) T1 gadolinium–enhanced MRI, and (**C**) sagittal T1 gadolinium-enhanced MRI at C4–6. These MRI findings showed severe canal stenosis due to the tumor. After surgery, the pathological diagnosis was meningioma.



A B

Figure 6. Intraoperative Tc-MsEP monitoring. **A,** There was no obvious waveform deterioration of the upper extremity. B, Compared with baseline (open arrow), the peak latency for the left gastrocnemius during tumor resection was delayed to 39 ms (control 33 ms), giving a delay of 18% (arrowhead). The bilateral abductor hallucis, quadriceps femoris, anal sphincter, and right hamstrings and gastrocnemius all showed an amplitude decrease of 70% or more from baseline. There was no obvious recovery in the waveform at the end of surgery (open arrowhead).

sensitivity 86%, specificity 98%, FPR 2%, and PPV 86% for prediction of paralysis postoperatively. This suggests that false positives can be decreased, and PPV can be increased by combining these two values. Previously, multimodality has been suggested to be important in intraoperative spinal cord monitoring, and Tc-MsEPs and D-waves may be an optimal combination.[4] However, there are many institutions that still use Tc-MsEP monitoring and it is not always possible to use D-wave monitoring. Therefore, by evaluating the latency in addition to the amplitude, it is possible to reduce the FPR and perform more optimal monitoring.

The study has several limitations, including relatively low sensitivity, difficulty with waveform evaluation in a case of dispersion or disappearance of the waveform, and evaluation of peak latency only. Furthermore, evaluation of a combination of an amplitude decrease and latency delay was only possible in a small number of patients. A sample size analysis carried out with G*Power software (v. 3.1.9, Heinrich-Heine-University, Dusseldorf, Germany) showed that the statistical power for all groups was 70.9%. An adequate sample size was not essential because the study was exploratory, but a calculated statistical power of more than 80% is generally optimal for a significant result. This suggests that larger-scale studies are needed. However, we were able to evaluate numerous waveforms from 1372 muscles in 70 cases. This allowed a delay in latency of 10% or more from baseline to be defined as an alarm point with high specificity, and a combination of the latency and amplitude could lead to a reduction of false positives. This is the first study to examine this combination of waveform amplitude and latency, and to demonstrate the efficacy of latency. We plan to perform a prospective study using these criteria, with evaluation of peak latency, onset latency, and the latency cutoff value.

In conclusion, we investigated the efficacy of a change of latency in Tc-MsEP monitoring. A latency delay of 10% or more from baseline had sensitivity of 86% and specificity of 97% for prediction of postoperative paralysis. A combination of a decrease in amplitude of 70% or more and a latency delay of 10% or more from baseline had specificity of 98%, FPR of 2%, and PPV of 86%. Use of the latency delay value did not have high sensitivity, but could allow reduction of the FPR and increase of the PPV. Further criteria and a cutoff for the latency delay are needed for more effective spinal cord monitoring.

➢ Key Points

- ❑ A retrospective study of amplitude and latency changes in monitoring of Tc-MsEP waveforms was performed in 70 patients undergoing spinal surgery.
- ❑ Relationships with postoperative paralysis were examined separately for latency delays of 5% or more and 10% or more, and in combination with a decrease in amplitude of 70% or more from baseline.
- ❑ Acceptable baseline Tc-MsEP responses were obtained from 1225 of 1372 muscles in the extremities (89.3%).

- A combination of a decrease in amplitude of 70% or more and a delay in latency of 10% or more from baseline gave good specificity and an FPR of 2% for prediction of postoperative paralysis.
- A combination of evaluation of latency and amplitude changes could lead to a reduction of false positives in Tc-MsEP waveform monitoring in spinal surgery.

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