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Comparison of Central Motor Conduction Time Using Transcranial Magnetic Stimulation and Evoked Spinal Cord Potentials Following Transcranial Electrical Stimulation in Compressive Cervical Myelopathy

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Abstract This study was performed to evaluate the accuracy of level diagnosis of cervical myelopathy using the measurement of the central motor conduction time (CMCT). In twenty-two patients with cervical myelopathy, the CMCT for the biceps brachii (Biceps) and the abductor digiti minimi (ADM) muscles were measured by subtracting the peripheral conduction time from the onset latency of the motor evoked potentials following transcranial magnetic stimulation. The peripheral conduction time was calculated by using T-waves for the Biceps and compound muscle action potentials and F-waves for the ADM. Results of the CMCT were compared with the evoked spinal cord potentials following transcranial electrical stimulation (TCE-ESCPs), which were recorded from the cervical posterior epidural space at each intervartebral level during surgery.

In all patients, abnormalities of both the TCE-ESCPs and the CMCT for the ADM were shown. Moreover, the CMCT for the Biceps was also prolonged in all six patients with abnormalities of the TCE-ESCPs at C3-4, although it was prolonged in just three patients in sixteen patients with abnormalities at C4-5 or C5-6. The CMCT for the Biceps had the significant correlation with the dysfunction of the spinal cord at C3-4. This is useful for clinical diagnosis of the disordered level of cervical myelopathy.

Introduction

Compressive cervical myelopathy is frequently observed during and after middle age, and often needs surgical treatment.[1] It is usually diagnosed by neurological examinations and radiological studies. Magnetic resonance imaging (MRI) is non-invasive and available for observation of the spinal cord. However, MRI gives no information on the function of the spinal cord and may lead to overdiagnosis of the compressed spinal cord.[2] It is occasionally difficult to determine if a compressed spinal cord on MRI is a symptomatic lesion of the spinal cord, especially in elder patients with multiple compressions. It is important to know the dysfunctional lesion of the spinal cord when choosing a method of the operation.

The motor evoked potentials (MEPs) following transcranial magnetic stimulation is a non-invasive method and valuable for evaluating the function of the central motor pathway.[3-5] It is possible to obtain estimates of the central motor conduction time (CMCT) by subtracting the peripheral motor conduction time from the latency of the MEPs.[6-8] The CMCT for muscles, which are innervated

by spinal motor neurons below the level of the lesion, should be prolonged. The CMCT for hand muscles is available for defining cervical myelopathy. Moreover, recording the CMCT for proximal upper limb muscles allows us to know the information pertaining to the function of the upper cervical cord.[9–12] These informations are useful for the level diagnosis of cervical myelopathy. In previous studies, the adequacy of the MEPs and the CMCT of cervical myelopathy were studied mainly by comparing radiological findings. However, the dysfunctional level of the spinal cord is not always correlated with the level of cord compression on radiological findings due to such disturbances as that of blood supply.[2,13–15] In order to find out the function of the corticospinal pathway, the evoked spinal cord potentials (ESCPs) following transcranial electrical stimulation has been recorded from epidural space in human.[16,17] It is a logical method for investigating the function of the motor pathways of the spinal cord.

In the present study, we measured the CMCT for the biceps brachii and the abductor digiti minimi, and compared the CMCT with the ESCPs following transcranial electrical stimulation (TCE-ESCPs). The purpose of this study is evaluating the adequacy of the CMCT for determining the level of the spinal dysfunction.

Materials and Methods

Twenty-two patients (mean age: 61 years old, range: 33-81 years old, seventeen men and five women) with clinical and radiological diagnosis of cervical myelopathy were studied. The causes of myelopathy were cervical spondylomyelopathy (CSM) in sixteen patients, ossification of posterior longitudinal ligament of cervical spine (OPLL) in three patients, and cervical disc herniation (CDH) in three patients. All patients with cervical myelopathy complained of numbness in the upper limbs and showed hyperreflexia in the lower limbs. There were no patients who had any previous history of other neurological disease. All the twenty-two patients underwent surgery. Operative procedures were selected based on radiological findings. Thirteen patients were treated by posterior decompressive surgery, and nine patients were treated by anterior decompressive surgery and spinal fusion. To obtain control values, the CMCTs of thirty-two normal subjects (mean age: 40 years old, range: 21-67 years old, nineteen men and thirteen women) were recorded. As for the TCE-ESCPs, eight subjects with thoracic spinal myelopathy and ten subjects with brachial plexus injuries but no lesion at the cervical spine (mean age 49 years old, range 20-74 years old, eleven men and seven women) were studied. All gave informed consent for the procedures and the studies had been approved by the ethical committee of Yamaguchi University School of Medicine.

MEPs

Transcranial magnetic stimulation of the motor cortex was achieved using a round 14 cm diameter coil (Magstim, Whitland, UK, Model 200). The center of the coil was held over the Cz position in the 10-20 international system. A clockwise current in the coil was delivered to stimulate the right hemisphere, and a counterclockwise current was used to stimulate the left hemisphere.[8] Stimulus intensity was defined as the intensity 20-30% above the threshold intensity (70-100% maximal output). The MEPs were recorded from the biceps brachii muscles (Biceps) and the abductor digiti minimi muscles (ADM) in more severely disabled side. Surface electrodes were placed in a belly-tendon position for the ADM. As for the Biceps, the reference electrode was placed in the humeral lateral epicondyle instead of the tendon. During stimulation, the target muscle was slightly voluntarily contracted in order to facilitate the responses.[6,18,19] The intensity of contraction was monitored by the loudspeaker of the surface EMG recordings. The MEPs signals were averaged 5-10 times.

CMCT

The conduction time from the motor cortex to the spinal motor neurons (central motor conduction time: CMCT) was calculated by

subtracting the peripheral conduction time (PCT) from the onset latency of the MEPs. Following examinations were done to obtain the PCT. For the ADM, the compound muscle action potentials (CMAPs) and the F-waves, following peripheral supramaximal electrical stimulation (square wave, 0.2 ms) of the ulnar nerve at the wrist, were recorded in the relaxed state. Twenty responses were collected, and the shortest latencies of the CMAPs and the F-waves were measured. As for the Biceps, the T-waves following stimulation by tapping the Biceps tendon were recorded. Five responses were collected, and the median value of onset latency was measured. The CMCT for the Biceps and the ADM were measured as follows. The CMCT for the ADM=latency of the MEP−(latency of CMAP + latency of F-wave+1)/2 ms.[8] The CMCT for the Biceps=latency of the MEP- (latency of T-wave+1)/2 ms.[20] In the calculation of the PCT of both muscles, we added 1 ms for the time of excitation at the spinal motorneuronal cell body. During the experiments of the MEPs and the PCT, the subjects were seated comfortably in the reclining chair.

ESCPs

During surgery, the TCE-ESCPs were recorded from the dorsal epidural space of the cervical spine using a bipolar technique, under general anesthesia with intravenously administered propofol. Transcranial electrical stimulation was achieved using the needle electrodes (13R21, Dantec, Denmark) put into the skull. The anode was placed at 7 cm lateral and 2 cm anterior to the Cz on a line joining the Cz with the external auditory meatus, where was approximately over the hand area of the motor cortex. The cathode was placed at opposite side to the Cz. The intensity of stimulation was the range from 70 mA to 99 mA and the duration was 0.2 ms.

In nine patients treated by anterior surgery, a catheter electrode with 5 recording tips at an interelectrode distance of 15 mm (UKG-100-5PM, Unique Medical Co., Japan) was inserted into the dorsal cervical epidural space for the purpose of the monitoring of the spinal cord during surgery.[21] In control subjects with brachial plexus injuries, this electrode was inserted to assess the continuity of nerve roots using the ESCPs following cervical nerve root stimulation.[22] In control subjects with thoracic myelopathy, an electrode was also inserted for the purpose of the monitoring of the spinal surgery using ECSPs following spinal cord stimulation.[21] The catheter electrode was inserted percutaneously into the midline of the dorsal cervical epidural space from the high thoracic level under fluoroscopic guidance on the day before surgery, while the patient was conscious. The highest electrode was advanced either to C2-3 or C3-4 disc level, and each of the electrodes was approximately put at the intervertebral disc level. Differential recordings were obtained bipolarly from four recording electrodes, using the 15 mm distal electrode as the reference.

In thirteen patients treated by posterior surgery, the TCE-ESCPs were recorded by needle electrodes (13R21, Dantec, Denmark). The active needle electrode was put directly into the yellow ligament at each interlaminar space of C2-3 to C6-7 during surgery. The reference needle electrode was put at one distal interlaminar space of the active electrode. The TCE-ESCPs were recorded before surgical decompression of the spinal cord.

In nine patients with inserted epidural electrodes, the ESCPs following transcranial magnetic stimulation (TCM-ESCPs) were also recorded simultaneously with the MEPs during consciousness without anesthesia on the day before surgery. At least two waves were redorded and superimposed in recording the TCM-ESCPs. The subjects were laid on the comfortable table for recording the TCM-ESCPs.

All signals of MEPs, CMAPs, F-waves, T-waves and ESCPs were amplified, filtered between 20 and 3000 Hz, and stored by using a standard electromyograph (Counterpoint, Dantec, Denmark or Nicolet Viking, Nicolet Biomedical, USA).

Results

Control Subjects

In control subjects of the CMCT, the CMCT for the Biceps was 3.8±0.5 ms (the latency of MEPs: 11.5±0.8 ms, T-waves: 14.5±0.7 ms),

and the CMCT for the ADM was 4.0±1.0 ms (the latency of MEPs: 19.5±1.5 ms, CMAPs: 3.3±0.6 ms, F-wave: 26.8±1.6 ms). Abnormal prolongation of the CMCT was set at 2.5 SD beyond the mean of the control values (beyond 5.05 ms for the Biceps and 6.50 ms for the ADM).

In all eighteen control subjects of the TCE-ESCPs, only one component (N1) of the TCE-ESCPs was recorded at each disc level from C2-3 to C6-7. The negative peak latency of the N1 at each disc level was 2.8±0.2 ms at C2-3, 3.1±0.2 ms at C3-4, 3.3±0.3 ms at C 4-5, 3.5±0.4 ms at C5-6, and 3.8±0.4 ms at C 6-7. Moreover, the amplitude of the TCE-ESCPs at each level was evaluated by the ratio of the amplitude of N1 to that of one proximal level. The amplitude of N1 was obtained by the distance between N1 and the point, which was intersected by the perpendicular formed by N1 and the line connected between the first positive peak (P1) and the second positive peak (P2). In control subjects, the ratio of the N1 amplitude was 88±18% at C3-4, 84±11% at C4-5, 77±12% at C5-6, and 65±19% at C6-7. Decreases of the amplitude were set so that ratios below 50% at C3-4, C 4-5 and C5-6, and below 25% at C6-7 were abnormal.

Patients with Cervical Myelopathy (Table 1)

CMCT

The CMCT for the ADM was significantly prolonged (from 7.15 ms to 19.55 ms, mean: 12.01 ms) in all twenty-two patients. Moreover, in nine patients, the CMCT for the Biceps was also prolonged (from 5.30 ms to 7. 85 ms, mean: 6.26 ms).

TCE-ESCPs

In all twenty-two patients, one TCE-ESCPs component (N1) was recorded from the posterior epidural space at the highest level (C2-3 in eighteen patients, C3-4 in four patients). In all patients, abnormal amplitude (significantly decreased or absent) of the N1 was shown at some of disc levels from C3-4 to C5-6. The level of abnormal amplitude of the N1 was C3-4 in six patients, C4-5 in seven patients and C5-6 in nine patients.

Comparison of the CMCT and the TCE-ESCPs

In all twenty-two patients who showed abnormalities of the TCE-ESCPs at C3-4, C4-5 or C5-6, the CMCT for the ADM was markedly prolonged. In all six patients with abnormal TCE-ESCPs at C3-4, the CMCT for both the Biceps and the ADM were prolonged. In all seven patients with abnormal TCE-ESCPs

Table 1 Patients with Cervical Myelopathy

Case	Age	Sex	Diagnosis	MRI findings (spinal cord)	Electrophysiological findings												
					CMCT (ms)		TCE-ESCPs										
				Level of			Amplitude of N1 (μV)					Ratio of amplitude (%)				Lesion
				compression	Biceps	ADM	C2-3	C3-4	C4-5	C5-6	C6-7	C3-4	C4-5	C5-6	C6-7	
1	72	M	CSM	multilevel	7.85*	14.05*	6.0	NR	NR	NR		0*	-	-	-	C3-4
2	73	F	CSM	multilevel	5.30*	14.20*	6.2	NR	NR	NR		0*	-	-	-	C3-4
3	55	M	CSM	multilevel	8.90*	10.85*	15.5	6.3	3.8	2.5		41*	60	66	0	C3-4
4	81	F	CSM	multilevel	5.55*	11.60*	35.0	11.8	6.3	4.0		34*	53	64	0	C3-4
5	74	M	CSM	C3-4	6.70*	13.35*	16.3	7.3	6.0	NR		45*	82	0	-	C3-4
6	41	F	CDH	C3-4	5.55*	7.25*	16.8	6.2	NR	NR		37*	0	-	-	C3-4
7	76	M	OPLL	multilevel	3.40	13.95*	15.0	8.0	3.0	2.0	1.2	53	38*	67	60	C4-5
8	73	M	CSM	multilevel	4.85	12.80*	5.8	4.0	0.8	NR		69	20*	0	-	C4-5
9	62	M	CSM	C4-5,5-6	3.20	15.00*	46.0	29.0	10.0	NR		63	34*	0	-	C4-5
10	70	F	OPLL	multilevel	3.25	13.50*	24.0	20.0	6.2	NR		83	31*	0	-	C4-5
11	53	M	CSM	multilevel	4.00	7.15*	11.0	9.6	NR	NR		87	0*	-	-	C4-5
12	60	M	CSM	C4-5	3.55	13.95*	44.0	26.0	4.0	NR		59	15*	0	-	C4-5
13	67	M	CSM	C4-5,5-6	3.60	14.00*		19.8	4.5	3.6	1.7		23*	80	47	C4-5
14	56	M	CSM	C4-5	3.80	11.80*	11.0	11.0	10.0	4.0	2.0	100	91	40*	50	C5-6
15	62	M	CDH	C5-6	3.35	19.55*		19.4	12.0	4.0	NR		62	33*	0	C5-6
16	55	M	CSM	C4-5,5-6	3.85	7.20*		24.0	20.0	8.0	NR		83	40*	0	C5-6
17	70	F	CSM	multilevel	5.35*	13.00*	34.0	18.0	13.0	NR		53	72	0*	-	C5-6
18	33	M	CDH	C5-6	3.75	8.95*	26.0	22.0	17.4			85	79	23*	0	C5-6
19	35	M	CSM	C5-6	5.56*	12.25*		26.0	24.0	7.6	NR		92	32*	0	C5-6
20	56	M	CSM	C5-6	4.25	14.90*	17.5	17.5	12.5	3.2		100	71	26*	0	C5-6
21	59	M	CSM	multilevel	3.15	7.80*	7.5	7.5	5.6	2.5		100	75	45*	0	C5-6
22	62	M	OPLL	multilevel	5.55*	11.45*	32.5	32.0	25.0			98	78	30*	0	C5-6

CSM, cervical spondylomyelopathy
CDH, cervical disc herniation
OPLL, ossification of posterior longitudinal ligament
NR, non- response
* abnormal value

at C4-5 and six of nine patients with abnormal TCE-ESCPs at C5-6, the CMCT for the Biceps was normal though the CMCT for the ADM was prolonged. Typical cases are shown in Fig. 1 and 2. In three of nine patients with abnormal TCE-ESCPs at C5-6, the CMCT for both the Biceps and the ADM were prolonged.

TCM-ESCPs

In three patients (case15, 18, 19) who had

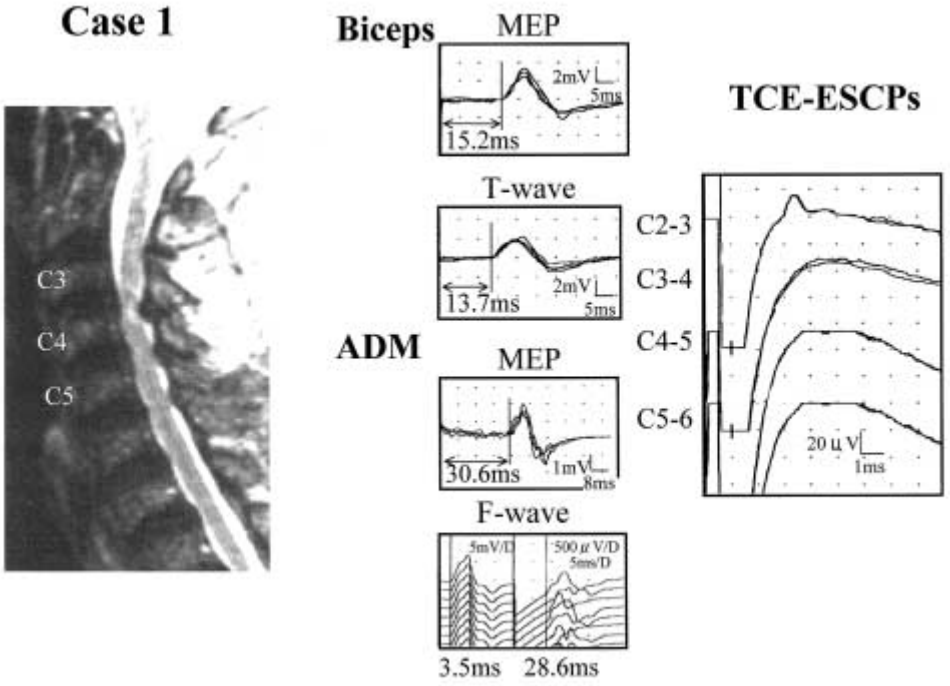

Fig. 1. Case 1: The CMCT for the biceps brachii was 15.2-(13.7+1)/2=7.85 ms, and that for the ADM was 30.6-(3.5+28.6+1)/2=14.05 ms. Both showed abnormal values. The TCE-ESCPs showed abnormal amplitude at C3-4.

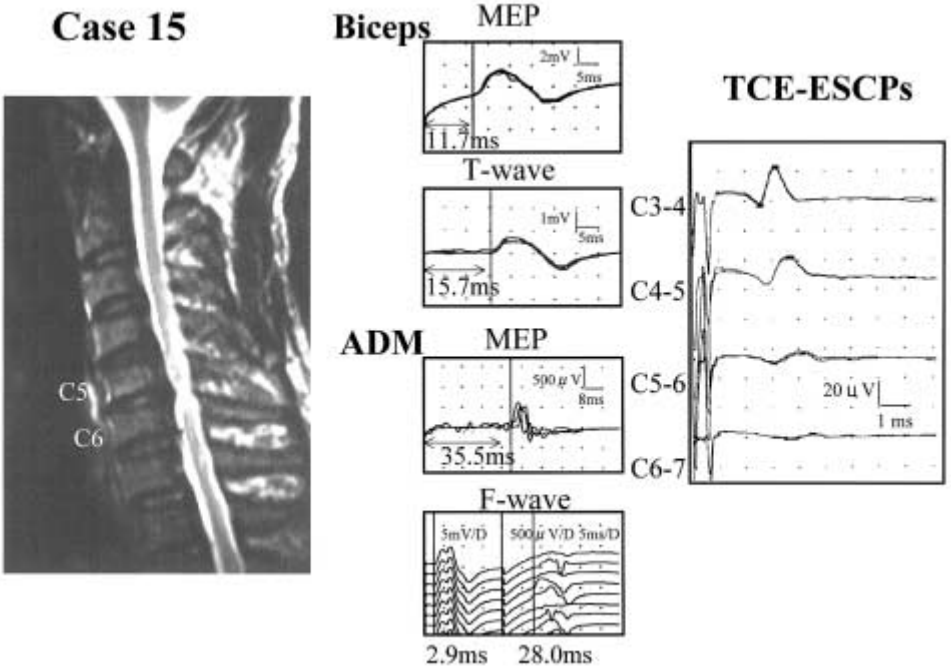

Fig. 2. Case 15: The CMCT for the biceps brachii was 11.7-(15.7+1)/2=3.35 ms, and that for the ADM was 35.5-(2.9+28.0+1)/2=19.55 ms. Only the CMCT for the ADM showed abnormality. The TCE-ESCPs showed abnormal amplitude at C5-6.

a single compression at C5-6 on MRI and abnormal TCE-ESCPs at C5-6, the TCM-ESCPs recorded at C3-4 disc level were compared. The C3-4 disc level was considered as the site where the anterior horn cells of the Biceps were localized. Results of the positive peak latency and the peak to peak amplitude of the TCM-ESCPs are shown in Table 2. As for the TCM-ESCPs, a significant difference of the latency of each component was not shown in three patients. However, in case 19, the amplitude of initial component was obviously smaller than that of other patients. As for the CMCT for the Biceps, only case 19 showed an

Table 2 TCM-ESCPs at C3-4 and CMCT for the Biceps

Case	TCM-ESCPs at C3-4								CMCT (ms)
	Latency (ms)				Amplitude (μV)				
	P1	P2	P3	P4	P1-N1	P2-N2	P3-N3	P4-N4	Biceps
15	2.3	3.8			21	13			3.35
18	2.5	3.3	4.2	4.8	20	14	2	10	3.75
19	2.0	3.3	4.7	5.9	10	10	17	20	5.56

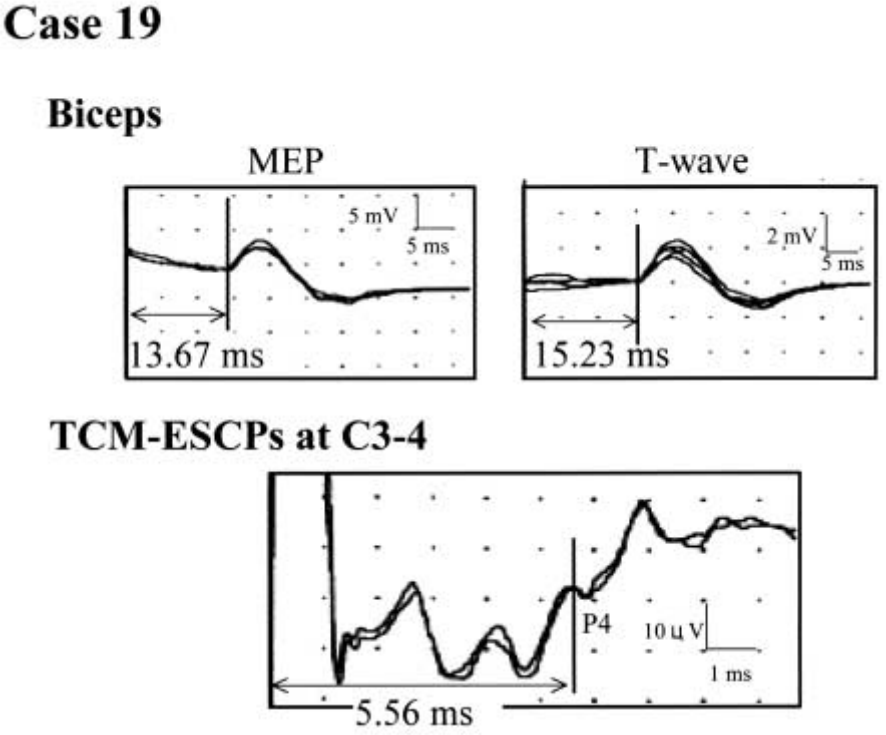

Fig. 3. Case 19: The CMCT for the biceps brachii was 13.67-(15.23+1)/2=5.56 ms. The CMCT showed abnormal prolongation, and it was approximated to the onset latency of the fourth component (P4) of the TCM-ESCPs at C3-4.

abnormal value. The responses of the Biceps and the TCM-ESCPs at C3-4 of case 19 are shown in Fig. 3.

Discussion

The CMCT for upper limb muscles using transcranial magnetic stimulation allows us to assess the function of the central motor pathway without the invasion to the subject, and has proven to be a reliable tool for diagnosing cervical myelopathy.[9–12] Moreover, a correlation between the CMCT for upper limb muscles and the dysfunctional lesion of the spinal cord was investigated in previous studies.[11,12] Lazzaro et al. studied

in fifteen patients with a single compression of the cervical spinal cord on MRI, and reported that the CMCT for the Biceps was prolonged in all five patients with a compression at C2-3 or C3-4 disc level, but it was normal in all ten patients with a compression at C4-5 or C5-6 disc level.[11] Tavy et al. examined the CMCT for the Biceps in nine patients with cervical myelopathy, and compared them with the disc level of the most severe stenosis on the myelography.[12] They reported that the CMCT for the Biceps was prolonged in seven of nine patients. In seven patients with prolonged CMCT for the Biceps, the severe stenosis was shown at C3-4 in six patients and at C4-5 in one patient. Both two patients with normal CMCT for the Biceps had the severe stenosis at C5-6. The significant correlation between the CMCT for the Biceps and higher cervical compressions on radiological findings was demonstrated in previous studies.[11,12] However, cervical myelopathy is caused not only by the direct cord compression but also by the vascular insufficiency. Therefore the dysfunctional level of the spinal cord is not always correlated with the level of cord compression on radiological finding.[15] In evaluating the function of the motor pathways of the spinal cord, electrophysiological studies are more accurate than radiological studies. In the present study, we recorded the evoked spinal cord potentials following transcranial electrical stimulation (TCE-ESCPs) to detect the dysfunctional level of the motor pathway. Direct transcranial stimulation of the motor cortex produces corticospinal electrical potentials at all levels of the spinal cord.[4] Recording these descending volleys (D-wave and I-waves[23]) of the spinal cord, following transcranial stimulation, can provide information regarding the function of the motor pathways of the spinal cord. In the present study, we could determine the dysfunctional level of the motor pathway using the TCE-ESCPs.

Moreover, in previous studies, the CMCT was calculated by subtracting the PCT that was obtained using the magnetic stimulation over the cervical spine.[11,12] But this method makes the CMCT include a proximal motor root conduction time, because the magnetic stimulation over the cervical spine excites motor roots at their spinal foramina.[24] In the present study, the PCT was obtained by using T-wave for the Biceps and F-wave for the ADM in order to prevent the CMCT from including a proximal motor root conduction time.[8,20]

When it is presumed that anterior horn cells innervating the Biceps were located mainly in C5 spinal segment, which corresponds to C3-4 disc level, the CMCT for the Biceps should be prolonged in patients with abnormal TCE-ESCPs at or above C3-4. In the present study, when the spinal segmental level of the Biceps was supposed to be C5 (C 3-4 disc level), for the cervical myelopathy at C3-4, the sensitivity of prolonged CMCT for both the Biceps and the ADM was 100% and specificity was 81.25%. Similar to previous studies,[11,12] the prolongation of the CMCT for the Biceps showed a significant correlation with the dysfunction of the motor pathways at C3-4 disc level.

However, in three of nine patients with abnormal TCE-ESCPs at C5-6, the CMCT for the Biceps were prolonged though the TCE-ESCPs at C3-4 were normal. One of three patients showed a single compression at C5-6 on MRI. In this patient, the TCM-ESCPs was also recorded during consciousness. A single magnetic cortical stimulation, similar to the electrical stimulation, can produce multiple descending potentials in the human pyramidal tracts.[25–27] Kaneko et al. demonstrated that, in normal subjects with voluntary contraction, the CMCT for the ADM corresponded best to the measured mean onset latency of the second component of the TCM-ESCPs at C6 - C6-7. This is due to the fact that the spinal motor neurons require two descending volleys following magnetic cortical stimulation in order to fire.[28] Moreover, Ofuji et al. found that the CMCT for the Biceps using T-wave was close to the mean onset latency of the second component of the TCM-ESCPs at C3-4 in normal subjects.[20] However, in our patient (case 19), prolonged CMCT for the Biceps was approximated to the onset latency of the fourth component of the TCM-ESCPs at C3-4. As compared with other patients (case 15 and case 18) who had normal CMCT for the Biceps and abnormal

TCE-ESCPs at C5-6, the amplitude of initial component of the TCM-ESCPs was obviously smaller in case 19. If the initial descending volley is reduced in size, it may be unable to discharge the motor neurons without temporal summation.[28,29] Our results suggest that the initial three components of the TCM-ESCPs may be too small to activate the spinal motor neurons with temporal summation and to elicit the MEPs in the Biceps. The insufficient intensity of transcranial magnetic stimulation should be responsible for this phenomenon.

In conclusion, this study proved that recording the CMCT for the Biceps and the ADM is useful for finding cervical myelopathy and detecting high cervical myelopathy. The CMCT could be available method for choosing the operation method, particularly in the patient who shows multiple compressions on MRI.

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