Research article

Effects of differences in age and body height on normal values of central motor conduction time determined by F-waves

Yasuaki Imajo, Tsukasa Kanchiku, Hidenori Suzuki, Yuichiro Yoshida, Masahiro Funaba, Norihiro Nishida, Kazuhiro Fujimoto, Toshihiko Taguchi

Department of Orthopaedic Surgery, Yamaguchi University Graduate School of Medicine Yamaguchi, Japan

Objectives: To investigate the effect on central motor conduction time (CMCT) based on the relationship between age and height in normal subjects.

Design: Retrospective study.

Methods: One hundred and ninety nine normal subjects (107 men and 92 women; mean age 39.0 ± 16.4 years; mean height 164.5 ± 8.8 cm) participated in the study. The approximate ages of subjects were as follows: 82 (20–29 years old), 32 (30–39 years old), 32 (40–49 years old), 28 (50–59 years old), and 25 (≥ 60 years old). The heights of 9, 49, 79, 53, and 9 subjects were <150 cm, 150–160 cm, 160–170 cm, 170–180 cm, and >180 cm, respectively. CMCT- abductor digiti minimi (ADM) and abductor hallucis (AH) were calculated by subtracting the peripheral motor conduction time (PMCT) from the onset latency of motor evoked potentials (MEPs) evoked by transcranial magnetic stimulation. PMCT was calculated from the latencies of the compound muscle action potentials (CMAPs) and F-waves as follows: (latency of CMAPs + latency of F-waves -1)/2.

Outcome measures: CMCT-ADM and CMCT-AH.

Results: The normative values were 5.2 ± 0.8 ms and 11.8 ± 1.3 ms for CMCT-ADM and CMCT-AH, respectively. CMCT-ADM was not significantly correlated with age ($P = 0.196$) and body height ($P = 0.158$). CMCT-AH had significantly positive, linear correlations with age and body height (CMCT-AH = $0.014 \times \text{age} + 10.971$, $P = 0.011$, $R = 0.179$ and CMCT-AH = $0.026 \times \text{body height} + 7.158$, $P = 0.010$, $R = 0.182$).

Conclusions: We suggest normative values of 3.2–7.2 ms in CMCT-ADM for subjects exerting slight effort on ADM regardless age and body height. CMCT-AH had significantly positive, linear correlations with age and body height.

Keywords: Central motor conduction time, Age, Body height, F-wave, Normative values

Introduction

Central motor conduction time (CMCT) is used to electrophysiologically evaluate corticospinal tract function and is also very useful for diagnosing disorders of the corticospinal tract. CMCT is noninvasive and safe for subjects when used to investigate lateral corticospinal tract function. However, there are few studies regarding the normal values of CMCT.^{1–4} The conduction time for the corticospinal tract is believed to be affected by body height, since it is dependent on the length of the conduction pathway. It is unclear whether normal values of CMCT can be adapted to people of different heights, or whether

aging affects the conduction time for the corticospinal tract; to our knowledge, no studies have reported age or height correlations with CMCT. Mano *et al.* showed that corticospinal tract conduction time was not correlated with age, whereas Eisen *et al.* reported that the conduction time was delayed in older subjects.^{4,5} The purpose of this study was to investigate CMCT based on the relationship between age and height in normal subjects.

Materials and Methods

One hundred and ninety-nine normal subjects (107 men and 92 women; mean age 39.0 ± 16.4 years; mean height 164.5 ± 8.8 cm) participated in the study. The approximate ages of subjects were as follows: 82 (20–29 years old), 32 (30–39 years old), 32 (40–49 years old),

Correspondence to: Yasuaki Imajo, Department of Orthopaedic Surgery, Yamaguchi University Graduate School of Medicine, 1-1 Minami-kogushi, Ube, Yamaguchi, 755-8505, Japan. Email: i-yasuak@yamaguchi-u.ac.jp

28 (50–59 years old), and 25 (≥ 60 years old). The height of 9, 49, 79, 53, and 9 subjects were <150 cm, 150–160 cm, 160–170 cm, 170–180 cm, and >180 cm, respectively. We interviewed the subjects to obtain their medical history before enrolling them into this study. None of the subjects had any history of central nervous system disorders, peripheral neuropathies, other neuromuscular diseases, or diabetes mellitus. Informed consent for participation in our study was obtained from all subjects. This study was approved by the institutional review board of Yamaguchi University Hospital.

Measurement of CMCT

Self-adhesive surface recording electrodes were placed on the target muscles using a standard belly-tendon method. Motor evoked potentials (MEPs) from abductor digiti minimi (ADM) and abductor hallucis (AH) on the left side were recorded during voluntary contraction. Transcranial magnetic stimulation (TMS) was delivered using a round 14-cm outer diameter coil (Magstim, Machida City, Tokyo). Transcranial stimulation was conducted with the stimulation coil positioned flat on the scalp and its center over Cz (international 10/20 system) with ADM. The coil center was over Fz for recording from AH. A clockwise current in the coil, as viewed from above, was used to stimulate the right hemisphere. The magnetic stimulus intensity was set at 20% above the threshold of the MEPs during voluntary contraction, which was monitored by audiovisual feedback of the raw electromyogram. We specified that the raw electromyogram should continually maintain contractions at approximately 10–20% of the maximal force during slight voluntary contractions. All stimuli were repeated at least four times, and all potentials were superimposed.

Compound muscle action potentials (CMAPs) and F-waves were also recorded following supramaximal electric stimulation (square wave 0.2 ms) of the ulnar nerves of the wrist and the tibial nerves of the ankle on the left side. Sixteen serial responses were obtained and the shortest latency of the F-waves was measured. All of

the muscle responses were amplified, filtered by 5–5000 Hz, and recorded using a standard electromyograph (Viking Select; Nicolet Biomedical Madison, Wisconsin, USA). The peripheral motor conduction time (PMCT), excluding the turnaround time at the spinal motor neuron (1 ms), was calculated from the latencies of CMAPs and F-waves as follows: (latency of CMAPs + latency of F-waves -1)/2.⁴

The conduction time from the motor cortex to the spinal motor neurons (such as the CMCT) was calculated by subtracting PMCT from the onset latency of the MEPs.

The latencies of the F-wave, MEPs, and CMCT measured to the left and right were treated as one because no obvious difference was found between them.³ Therefore, we evaluated the left corticospinal tract using only CMCT in this study.

Statistical analysis

The latency of MEPs, PMCT, and CMCT, as well as the shortest latency of F-wave, were evaluated in subjects. A simple linear regression was conducted to investigate the relationship between each conduction parameter (F-wave latency, which was recorded from ADM and AH; MEPs latency, which was recorded from ADM and AH; CMCT-ADM; and CMCT-AH) and age, as well as between these parameters and body height. For simple linear regression analysis, the correlation coefficient was expressed as an R value. P values of <0.05 were considered statistically significant.

Results

Relationship between age and each latency (Table 1)

The normative value was 5.2 ± 0.8 ms in CMCT-ADM and 11.8 ± 1.3 ms in CMCT-AH.

No significant correlation was founded between each parameter recorded from ADM and age (F-wave latency: $P = 0.704$, MEPs latency: $P = 0.951$, CMCT-ADM: $P = 0.196$) (Figure 1).

All measured conduction parameters recorded from AH had a significantly positive, linear correlations

Table 1 Normative data. Relationship between age and each latency (F-wave, MEPs, and CMCT)

Recorded muscle		Total (n = 199)	Age				
			20s (n = 82)	30s (n = 32)	40s (n = 32)	50s (n = 28)	60s or older (n = 25)
ADM	F-wave	24.7 ± 1.9	24.7 ± 2.0	24.4 ± 1.7	24.7 ± 1.9	24.6 ± 1.9	24.8 ± 1.9
	MEPs	18.5 ± 1.3	18.6 ± 1.5	18.5 ± 1.1	18.5 ± 1.3	18.3 ± 1.0	18.6 ± 1.3
	CMCT	5.2 ± 0.8	5.3 ± 0.8	5.4 ± 0.9	5.2 ± 0.8	5.1 ± 0.5	5.2 ± 0.9
AH	F-wave	44.1 ± 3.2	44.1 ± 3.6	43.1 ± 2.6	45.3 ± 2.7	44.7 ± 3.6	45.2 ± 2.3
	MEPs	35.2 ± 2.3	35.1 ± 2.1	34.8 ± 2.3	35.9 ± 2.3	35.9 ± 2.3	36.5 ± 2.3
	CMCT	11.5 ± 1.3	11.3 ± 1.1	11.6 ± 1.6	11.6 ± 1.5	11.5 ± 1.1	11.9 ± 1.3

MEPs: motor evoked potentials, CMCT: central motor conduction time, ADM: abductor digiti minimi, AH: abductor hallucis.

Figure 1 Distribution of cases according to subject age. Relationship between CMCT-ADM and age. F-wave and MEPs were recorded from ADM. CMCT-ADM was normally distributed. CMCT-ADM was not significantly correlated with age ($P = 0.196$). ADM: abductor digiti minimi, CMCT: central motor conduction time.

with age (F-wave latency = $0.030 \times \text{age} + 43.220$, $P = 0.033$, $R = 0.15$, MEPs latency = $0.036 \times \text{age} + 34.077$, $P = 0.0002$, $R = 0.260$, CMCT-AH = $0.014 \times \text{age} + 10.971$, $P = 0.011$, $R = 0.179$) (Figure 2).

With regard to the relationship of age and CMCT (ADM and AH), we tested for the difference of regression line slopes after partitioning the data at 60 years of age. We did not find statistically significant difference in the slopes.

Relationship between body height and each latency (Table 2)

Two measured conduction parameters, except those for CMCT-ADM that were recorded from ADM, had significantly positive linear correlations with body height (F-wave latency = $0.141 \times \text{body height} + 1.494$, $P < 0.001$, $R = 0.641$, MEPs latency = $0.083 \times \text{body$

height + 4.924 , $P < 0.001$, $R = 0.560$). No significant correlation was founded between CMCT-ADM and body height ($P = 0.158$) (Figure 3).

All measured conduction parameters recorded from AH had significantly positive linear correlations with body height (F-wave latency = $0.227 \times \text{body height} + 7.071$, $P < 0.001$, $R = 0.614$, MEPs latency = $0.145 \times \text{body height} + 11.626$, $P < 0.001$, $R = 0.564$, CMCT-AH = $0.026 \times \text{body height} + 7.158$, $P = 0.010$, $R = 0.182$) (Fig. 4).

Discussion

Two main methods are used to calculate CMCT; one uses magnetic root stimulation⁴⁻⁷ whereas the other uses F-waves.^{2-4,8,9} The CMCT calculated by subtracting the F-wave latencies from the latencies measured

Figure 2 Distribution of cases according to subject age. Relationship between CMCT-AH and age. F-wave and MEPs were recorded from AH. CMCT-AH was normally distributed. A significant and positive linear relationship was found between CMCT-AH and age (CMCT-AH = $0.014 \times \text{age} + 10.971$, $P = 0.011$, $R = 0.179$). AH: abductor hallucis, CMCT: central motor conduction time.

Table 2 Normative data. Relationship between body height and each latency (F-wave, MEPs, and CMCT)

Recorded muscle		Body height				
		139 ≤ <150 (n = 9)	150 ≤ <160 (n = 49)	160 ≤ <170 (n = 79)	170 ≤ <180 (n = 53)	180 ≤ (n = 9)
ADM	F-wave	22.8 ± 2.3	23.2 ± 1.2	24.5 ± 1.5	26.0 ± 1.6	27.5 ± 1.0
	MEPs	17.4 ± 1.4	17.7 ± 0.9	18.4 ± 1.1	19.3 ± 1.1	20.2 ± 1.1
	CMCT	5.1 ± 0.9	5.2 ± 0.9	5.3 ± 0.8	5.4 ± 0.7	5.4 ± 0.5
AH	F-wave	40.8 ± 4.2	42.7 ± 2.4	43.9 ± 2.4	46.2 ± 2.5	50.7 ± 2.6
	MEPs	33.4 ± 2.7	34.2 ± 2.1	35.2 ± 1.7	36.7 ± 1.8	39.2 ± 1.6
	CMCT	11.2 ± 1.3	11.1 ± 1.2	11.6 ± 1.3	11.8 ± 1.3	11.9 ± 1.0

MEPs: motor evoked potentials, CMCT: central motor conduction time, ADM: abductor digiti minimi, AH: abductor hallucis.

Figure 3 Distribution of cases according to subject body height. Relationship between CMCT-ADM and body height. F-wave and MEPs were recorded from ADM. CMCT-ADM was not significantly correlated with body height ($P = 0.158$). ADM: abductor digiti minimi, CMCT: central motor conduction time.

to ADM after transcranial stimulation are slightly shorter than that obtained after magnetic root stimulation.⁴ This difference is due to the fact that the

F-wave represents the latency to the alpha motor neuron, whereas the site of magnetic root excitation is separate to that of the spinal root exit. CMCT measured

Figure 4 Distribution of cases according to subject body height. Relationship between CMCT-AH and body height. F-wave and MEPs were recorded from AH. A significant and positive linear relationship was found between CMCT-AH and body height ($\text{CMCT-AH} = 0.026 \times \text{body height} + 7.158$, $P = 0.010$, $R = 0.182$). AH: abductor hallucis, CMCT: central motor conduction time.

using magnetic root stimulation is the conduction time from the motor cortex to the cervical neuroforamina.⁷ CMCT measured using F-waves is the conduction time from the motor cortex to the spinal motor neurons. We chose CMCT from the F-waves for this study because we wanted to accurately evaluate the function of the corticospinal tract. The fibers activated by the magnetic stimulator and those activated by F-waves are not always same. F-waves were inconstant, varying in latency and amplitude, and often not present with each stimulus. When the nerves are stimulated at least 10 times, the shortest F-wave latency was constant in normal subjects. We considered that large cells in anterior horn were activated.

With regard to these fibers activated by the magnetic stimulator, patients with Shy-Drager syndrome have the severe involvement of corticospinal tracts in histological and neurological findings. But CMCT was normal for patients with Shy-Drager syndrome. Small diameter medullated nerve in corticospinal tracts was affected for patients with Shy-Drager syndrome.¹⁰ On the other hand, CMCT was prolonged for patients with amyotrophic lateral sclerosis (ALS). Large diameter medullated nerve in corticospinal tracts was affected for patients with ALS.^{11,12} CMCT was reflected by large diameter medullated nerve in corticospinal tracts. Therefore, we considered that fibers activated by the magnetic stimulator activated large cell in anterior horns.

Rossini *et al.* reported the relationship between the latency and coil position.¹³ In coil position, only a small proportion of corticospinal neurons are directly stimulated (=minimal latency and lowest threshold), whilst corticocortical axons would be excited by the tangential components of current flow. This explains why when centering the coil on the vertex latencies are longer and thresholds higher than when placing the coil laterally over the appropriate parietofrontal scalp region contralateral to the target muscle (=hot spot).

Voluntary contraction of muscles enhanced MEP amplitudes and shortens the latencies.¹⁴ Ravnborg M *et al.* studied the effect of increasing voluntary muscle contraction on the CMCT and MEP amplitudes to establish the importance of standardization of the facilitation of central motor conduction measured by magnetic stimulation.¹⁵ Muscle force was indirectly assessed from the integrated electrical muscle activity and expressed as the root mean square (RMS) and varied from 0–40% of maximal activity. The CMCT decreased during increasing muscle contraction, reaching constant values at approximately 10–20% RMSmax. Similarly, the increases of MEP amplitude tapered off at about the same RMS level. MEPs were

recorded per ADM and AH during slight voluntary contraction, which was monitored by audio-visual feedback of the raw EMG. We specified that the raw electromyogram should continually maintain contractions at approximately 10–20% of the maximal force during slight voluntary contractions. Therefore, we considered that CMCT was reliable.

Peripheral motor conduction velocity is reported to be affected by age.^{1,16} Some authors have reported the importance of age-related peripheral nerve changes, such as progressive fiber loss and segmental demyelination.¹⁷ A significant difference was found between the F-wave latency and MEPs latency recorded from AH and age. However, no significant difference was found between the F-wave latency and MEPs latency recorded from ADM and age. This discrepancy may reflect the length of the motor conduction pathway. Functional changes in the peripheral nervous system with age are not uniform.⁴ Changes in the peripheral nervous system start earlier than the central nervous system, and the conductivity of the pyramidal tract is preserved.⁴ Terao *et al.* quantitatively analyzed the myelinated fibers in the lateral corticospinal tract at the levels of the sixth cervical segment in 20 patients between 19 and 90 years of age, and who had died of non-neurological diseases.¹⁸ The results showed that the density of the small myelinated fibers was significantly lowered with advancing age, whereas that of the large myelinated fibers was not significantly decreased with age, although it showed a slight tendency to age-dependent decline. CMCT was used to evaluate large fibers in the lateral corticospinal tracts.¹⁸

In this study, no significant correlations were found between CMCT- ADM and age or between CMCT-ADM and body height. However, there were significant correlations between CMCT-AH and age, and between CMCT-AH and body height. Claus reported that CMCT to the upper extremities is not significantly affected by age or height, whereas CMCT to the lower extremities is significantly affected by height.¹ However, the study by Claus did not include any patients aged 60 years or older. In the present study, excluding normal subjects aged 60 years or older, no significant correlation was founded between CMCT-AH recorded from AH and age (CMCT-AH: $P = 0.07$). Thus, our results were consistent with Claus' results.

Mano *et al.* reported no significant difference in CMCT-ADM between aged subjects and young subjects.⁴ Although the older subjects were shorter than the younger subjects, the distance from Cz to the seventh vertebra, which is known to be relatively constant, did not differ between age groups,⁴ which is

consistent with our results. Matsumoto et al. reported that corticoconus motor conduction time (CCCT) was less affected by aging than by PMCT.⁶ The reason for this can be explained by anatomy; the brain and spinal cord are protected by the cranial bones and the vertebral column, respectively, but peripheral nerves are directly and easily affected by minor trauma.⁶ CCCT was the conduction time from the motor cortex to the cauda equina at the L1 spinous process. CCMC includes the synaptic delay between the corticospinal tract and the spinal motor neurons, and there may not be a significant difference in the correlation between this synaptic delay and age.

At present, Japan has a rapidly aging population and is considered the only “super-aging society” among advanced countries in 2010.¹⁹ Degenerative diseases such as compressive cervical myelopathy (CCM) and compressive thoracic myelopathy (CTM), are commonly found in super-aging societies.²⁰

CCM and CTM can be diagnosed using neurological findings such as deep tendon reflex, sensory disturbance, motor weakness, and radiological findings including plain radiographs, magnetic resonance imaging (MRI), and computed tomography (CT). It was sometimes difficult to diagnose CCM and CTM using neurological findings in elderly patients with neurological disorders, such as diabetic and entrapment neuropathies, or degenerative osteoarthritis in lower limbs. Some elderly subjects are diagnosed with asymptomatic spinal cord compression in radiological findings.²¹

Some authors reported that measurement of CMCT was valuable for diagnosis of CCM and CTM.^{2,3,22} CCM consists of cervical spondylotic myelopathy (CSM), ossification of the posterior longitudinal ligament (OPLL), and other degenerative disease. Some authors have reported that most patients with CSM were in their sixth and seventh decades by the time of surgery.²³ Most patients with OPLL develop symptoms in their fifties.²⁴ Diagnosis from symptoms or neurologic findings can be difficult when elderly patients with CCM and CTM have coexisting myelopathy and peripheral neuropathy. MRI shows spinal cord compression in as many as 25% of these patients, especially the elderly, who often have no clinical symptoms or signs of myelopathy.²⁵ The function of the corticospinal tract can be accurately evaluated using CMCT, thereby excluding asymptomatic spinal cord compression on MRI. Kaneko K *et al.* compared CMCT following TMS and evoked spinal cord potentials (ESCPs) following transcranial electric stimulation to investigate the mechanism of the prolonged CMCT in CCM.² Prolonged CMCT may occur with only slight

slowing of the conduction in the corticospinal tract in CCM. Impaired temporal summation of multiple descending potentials following TMS can produce delays in motor neuron firing, thus contributing to the mechanism of prolonged CMCT. Nakanishi *et al.* reported that CMCT prolongation was primarily due to corticospinal conduction block, rather than conduction delay.²⁶

Kaneko *et al.* reported that measuring of CMCT is an ideal, noninvasive diagnostic approach for patients with coexisting entrapment neuropathy and CCM.⁸ It is considered abnormal when this value exceeds the normal mean value by more than 2.5 SD; hence, an abnormally prolonged value is defined at approximately 7.2 ms in CMCT-ADM and at approximately 15.1 ms in CMCT-AH in our study. We suggest that patients with more than 7.2 ms in CMCT-ADM may have CCM and patients with less than 7.2 ms in CMCT-ADM and more than 15.1 ms in CMCT-AH may have CTM.

Nagashima *et al.* reported that prompt decompression surgery was required due to rapid deterioration after disease onset in the elderly.²⁷ Elderly patients aged 80 years or older regained approximately 40% of their function postoperatively. Patients with longer disease duration had worse outcomes. Surgical intervention should be performed in elderly patients with early-stage CCM. Funaba *et al.* reported that CMCT-ADM was useful for the CCM rostral to the C5-6 intervertebral level and diagnosis of patients with C6-7 myelopathy should include assessment of the CMCT-AH.²⁸ Therefore, we suggest that CMCT may be one useful factor to consider when evaluating patients with symptomatic spinal myelopathy. With regard to CCM, 7.2 ms cutoff value should be used for ADM regardless of age or body height. We suggest that normative values range from 3.2 ms to 7.2 ms in CMCT-ADM.

In future, we will analyze CMCT of patients undergoing surgery for CCM and CTM. In addition, we will detect the sensitivity, specificity, and accuracy of diagnosis when the 7.2 ms cutoff value is used for patients with CCM compared with that of the CMCT-ADM of patients undergoing surgery for CCM. We consider that our formulas may be very useful for predicting CMCT-AH according to age and body height, and in future research, we will use these formulas to assess the sensitivity, specificity, and accuracy of diagnosis compared with CMCT-AH of patients undergoing surgery for CTM.

Limitations

F-wave latencies, MEPs latencies, and CMCT may not apply to non-Japanese populations, children, or population that are 190 cm or taller. Average body height of

Japanese was almost same as that of Asian. But average body height of Japanese was more than 10 cm shorter than that of the Dutch and the Danes.^{29,30} Therefore, there may be significant difference between F-wave latencies, MEPs latencies, and CMCT of Japanese and these of the Dutch and the Danes. MEPs latencies and CMCT may not apply to normal subjects during rest. Also, MEPs latencies and CMCT may be different if the coil is used over hotspots instead of the vertex. Therefore, we should pay attention to the coil position.

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