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A novel approach for evaluating nerve function in healthy elderly persons: A pilot study

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Background: Motor nerve function decreases with age and can cause abnormalities in motor function. Using newly designed methods, we used evoked electromyograms to evaluate change in motor nerve function.


Material/Methods: Motor function was assessed by grip strength, timed up-and-go test, 5-m normal walk, and 5-m fastest walk. In addition, motor nerve conduction velocity was calculated by measuring latency differences (*NCV*) in elderly and young subjects. We also investigated motor nerve conduction velocity by correlation coefficient (*NCVCC*) and the difference between *NCV* and *NCVCC* (*DNCV*).

Results: Significant differences were observed in the motor function of elderly and young persons in grip strength, the timed up-and-go test, and the 5-m fastest walk; however, no difference was observed in the 5-m normal walk test. *NCVCC* was lower than *NCV* in both elderly and young. The correlation coefficient peak of the *NCVCC* calculation was lower in elderly than in young. A negative correlation was observed between correlation coefficient peak and *DNCV* in elderly subjects.

Conclusions: *NCVCC* compares the overall shape of compound muscle action potential and reflects not only the fastest motor unit, but also the motor nerve conduction velocity of other motor unit components. A significant negative correlation between *DNCV* and the correlation coefficient peak was observed only in elderly subjects, suggesting that older individuals, including those that maintain a high level of physical strength, experience a loss of motor nerve function. Thus, changes in motor nerve function among elderly persons can potentially be further examined for clinical use.

Key words: **nerve conduction velocity • compound muscle action potential • evoked electromyography • elderly person**

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Background

Nerves degenerate with age, which causes a decline in nerve conduction velocity [1–4]. Normally, this degeneration is slow; therefore, obvious symptoms affecting daily life do not suddenly appear. However, progression of degeneration causes functional disorders of sensory and motor nerves. Symptoms of sensory nerve disorders include numbness or pain in the hands and feet and dulling of the senses. Motor nerve disorders can cause abnormalities in motor function, including muscular weakness and abnormal motor skills.

Limiting age-related loss of motor function is vital in maintaining the capabilities of the elderly [5]. Although weakening of muscles in the upper and lower limbs is linked to decreased motor function in later life, reduced motor nerve function also leads to muscular weakening [6,7]. Motor function is required for daily living, including activities such as walking. The initial stages of motor function decline are exacerbated in the elderly when early decline in motor function leads to further disuse of muscles.

This decline is even more obvious in common chronic illnesses such as diabetes or entrapment neuropathy [8–11]. In their study of the nerve and muscle function of early-stage diabetes patients, Meijer et al used invasive needle electrodes to examine the muscle fiber conduction velocities through the muscle fibers of the tibialis anterior muscle. Although all the patients had normal muscle strength, half experienced a decline in motor and sensory nerves. In addition, the temporal dispersion of the muscle fiber conduction velocities was correlated with reduced sensory nerve conduction velocity [12]. Thus, even when damage occurs in a portion of the muscle fibers, other muscle fibers are believed to supplement the overall musculature. A similar process is thought to occur gradually in the elderly.

Initiatives to maintain and improve the daily lives of the elderly have consisted of exercises to improve muscle strength, endurance, and balance [13,14]. However, if declines in nerve function can be diagnosed early, an individualized training regimen may slow further declines. Early diagnosis and prevention of muscular atrophy from lack of use, as well as measures that maintain muscle strength, could improve and maintain motor function in the elderly.

Nerve degeneration is associated with changes in nerve conduction, which can be noninvasively analyzed using surface electrodes. When calculating nerve conduction velocity, the compound muscle action potential (CMAP) of evoked electromyography (evoked EMG) can be thought of as a collection of action potentials that are generated by the large motor units of a muscle after the nerve is stimulated. To date, CMAP

has been primarily used to detect nerve function abnormalities by observing the amplitude of the CMAP (size) and calculating nerve conduction velocity from the latency differences in CMAP, which depend on the site of electrical stimulation. However, CMAP incorporates a variety of factors, including the action potentials of individual motor units, the relative position of the surface electrodes, and the number of active motor units [15]. The simulation of temporal dispersion caused by a conduction block and occurrence in a portion of motor units can be extrapolated using the CMAP configuration [16]. Studies have also identified CMAP components by examining single-fiber action potentials in laboratory animals [17]. A variety of possible methods have been used in the theoretical estimation of nerve fiber action potentials or CMAP. Because normalization requires a series of difficult and complex processing techniques, clinicians need a simple, straightforward generic processing method that encompasses the characteristics of CMAP waves.

We developed a small portable electrical stimulation device and an evoked myoelectric recording system. Using calculation software developed for this study, wave differences were examined by comparing correlation coefficients of the various CMAPs obtained from proximal and distal electrical stimuli as a pilot study. The nerve function of elderly and young persons was compared, and the spread of motor nerve conduction velocities of motor unit action potentials was estimated according to age.

Material and Methods

Subjects

The subjects were 24 individuals aged 64 years or older who had no history of neuromuscular disease and had normal activities of daily living (age 72 ± 6.7 years [mean \pm SD]; 5 males, 19 females, aged between 64 and 87 years). They were selected from the members of a club administered by the Tokyo municipality. In addition, 10 young persons (age 24.8 ± 5.8 years [mean \pm SD]; 6 males, 4 females, aged between 21 and 39 years) were evaluated. They were university students who consented to participate in this study. We prepared the experimental facility in consideration of the participating elderly persons and fewer young persons consented to participate (Table 1). Approval for the study was obtained from the Saitama Prefectural University Ethics Committee. Only individuals who gave informed consent for participation were included.

Measurement of motor function

Motor function measurements were collected in accordance with the "Appraisal standards for functional measures in

Table 1. Subject data and motor function.

	Older (n = 24)				Younger (n = 10)			
	Mean	SD	Max. value	Min. value	Mean	SD	Max. value	Min. value
Age (y)	72.0	6.7	87	65	24.8	5.8	39	21
Gender (male/female)	5/19				6/4			
Height (cm)	154.4	8.0	176	140	167.2	12.2	181	145
Weight (kg)	58.6	7.0	68.5	40	65.1	11.2	79	49
Grasp Strength (kg)	25.8	4.9	39	20	41.9	13.4	59	26
Timed Up and Go (s)	5.71	1.09	8.02	3.76	4.74	1.27	7.31	3.19
5 m Normal Walk (s)	3.59	0.48	4.44	2.72	3.45	0.54	4.37	2.88
5 m Fastest Walk (s)	2.69	0.39	3.46	2.00	2.19	0.37	2.58	1.72

independent elderly people” submitted by the Ministry of Health, Labor, and Welfare of Japan. The method was demonstrated to the subjects before beginning the procedure, and the measurement process was begun only after the subjects adequately understood the procedure and preliminary training. Subjects were informed of the measurement results, which corresponded to 1 of 5 evaluation levels that were calculated by using data from 3852 individuals. The measurer and assistant were also responsible for ensuring environmental safety. Four areas of motor function were measured:

1. *Grip strength*: grip strength of the dominant hand was tested as the subject stood with feet apart, taking care not to allow for any compensatory motion.
2. *Three-meter timed up and go test (TUG)*: the subject begins the test seated on a chair with back pressed against the back support, and the time taken to stand, walk over to a marker placed 3 m away, turn the marker over, and return to a sitting position was measured. The standard instruction given to all subjects was “return to the seat as fast as possible”.
3. *Five-meter normal walk*: the subject was asked to walk more than 8 m in total. The time taken from when a foot first crossed the 3-m mark until the foot crossed the end of the measurement area was measured. The standard instruction given to all subjects was “walk as you normally would in a straight line”.
4. *Five-meter fastest walk*: the subject was asked to walk more than 8 m in total, but this time the standard instruction given to all subjects was “walk as fast as possible in a straight line”.

Measurement of motor nerve function

Motor nerve conduction velocity was measured using an electrical stimulus device (distance between stimulus electrodes: 2.5 cm; TOP Surgical Mfg. Company, Tokyo, Japan). Subjects placed their dominant arm on a platform and the palm was

turned upward. Electrodes with a diameter of 7 mm (NE-1211, Nihon Kohden, Tokyo, Japan) were used, and the active and reference electrodes were placed on the venter of the abductor muscle of the little finger and 4 cm from this position, respectively. The central area 5 cm from the active electrode on the wrist was designated as the first stimulus area, and the central area 5 cm from the groove of the ulnar nerve was designated as the second stimulus area. The electrical stimulus wave interval was 0.3 ms, with the stimulus frequency was set at 1 s. The action potential was checked to ensure there were no changes over the course of 15 amplitudes, and electromyography (EMG) was recorded. The surface temperature of the stimulus area and venter were maintained at $33 \pm 0.5^\circ\text{C}$ (mean \pm SD, measured using an infrared thermometer; t826-T3, Testo, Germany, error $\pm 0.5^\circ\text{C}$). The recording frequency of the bio-amplifier (MEG-6108, Nihon Kohden, Tokyo, Japan; CMRR > 80 dB, input impedance 100 M Ω) was set at 5 Hz. The sampling rate was 10 000 samples/s, which were converted from analog to digital (NI 9215, National Instruments, Austin, TX, USA) and stored in a calculator. The mean was calculated for the EMG data obtained from the evoked potential of 10 stimulations. Motor nerve conduction velocity was calculated according to the latency differences between the first and second stimulus waves using equation (1):

$$NCV = D/TD1 \quad (1)$$

in which *NCV* refers to motor nerve conduction velocity, *D* to the distance between the first and second stimulus sites, and *TD1* to the latency difference between the starting points of the action potentials obtained from the evoked EMG of the first and second stimulus (upper and middle graphs of Figure 1).

Next, the time difference between the myoelectric waves (according to the correlation coefficient between the evoked EMG) was compared with the motor nerve conduction velocity

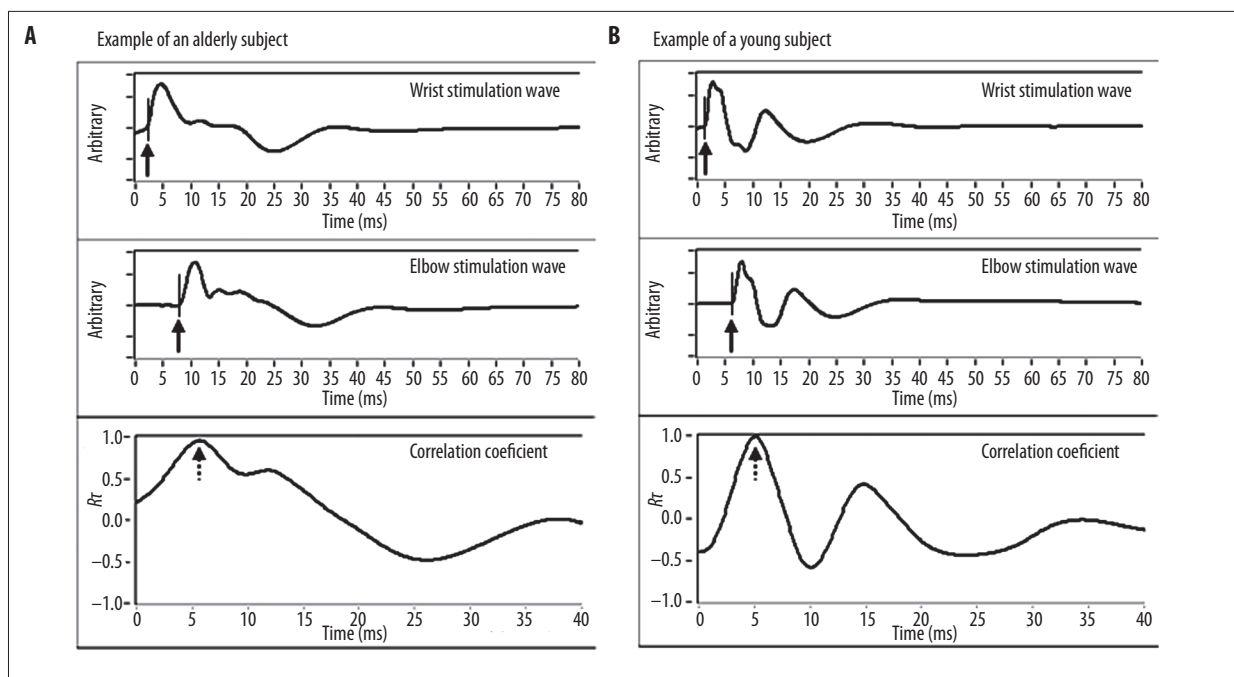


Figure 1. Example of calculating the motor nerve conduction velocity. This figure shows an example calculation of motor nerve conduction velocity using evoked electromyography (EMG) findings from an elderly and young subject. Motor nerve conduction velocity, NCV , is calculated using the latency difference from the wrist stimulation wave until the start of the action potential of the elbow stimulus (the time difference between solid lines is indicated by arrows in the upper and middle graphs). The correlation coefficient between the evoked EMG is calculated, and the motor nerve conduction velocity, $NCVCC$, is calculated on the basis of the time taken for the correlation coefficient R_t to reach its peak (R_t peak, indicated by the arrow in the lower graph). **(A)** NCV is 49.1 m/s, $NCVCC$ is 47.4 m/s, and R_t peaks at 0.95 for the elderly individual, while **(B)** NCV is 50 m/s, $NCVCC$ is 49 m/s, and R_t peaks at 0.99 for the young individual.

determined by equation (1). The correlation coefficient R_t , the time difference between the myoelectric wave, x , of the first stimulus and myoelectric wave, y , of the second stimulus, were calculated using equation (2):

$$R_t = \frac{\sum_{i=1}^N (x_i - \bar{X}) * (y_{i+\tau} - \bar{Y})}{\sqrt{\sum_{i=1}^N (x_i - \bar{X})^2 * \sum_{i=1}^N (y_{i+\tau} - \bar{Y})^2}} \quad (2)$$

here R_t is a normalized value between -1 and $+1$. N is the sample size dependent on the time of the electromyogram waves being studied, where the electromyogram wave time was set as 100 ms; therefore, sample size N was 1000 samples (100 ms \times 10 000 samples). However, during the initial stimulus period, the first 2 ms of the wave was disregarded because the stimulant electricity must first pass through the skin. \bar{X} and \bar{Y} are the means of x and y . $TD2$, the time from point 0 to the maximum value of R , is the time difference between x and y . The motor nerve conduction velocity under these conditions ($NCVCC$) can be determined using equation (3):

$$NCVCC = D/TD2 \quad (3)$$

where the distance, D , between the first and second stimulus sites is identical to NCV . The correlation coefficient of the motor nerve conduction velocity was calculated (lower graph of Figure 1). In addition, the peak of the correlation coefficient R_t (R_t peak) could be determined. To ensure reliability of the calculated values, only subjects with an R_t peak exceeding 0.9 were used in the analyses of motor nerve conduction velocity.

Because 2 separately calculated values for motor nerve conduction velocity were used, the difference between the calculated values, the ratio $DNCV$, was calculated using the following equation (4):

$$DNCV = (NCV - NCVCC)/NCV \quad (4)$$

The calculation software used for all of these processes was developed by LabVIEW Ver. 2010 (National Instruments, Austin, TX, USA).

Statistical analyses

Statistical processing was conducted using SPSS Ver. 17.0 (SPSS Inc., Chicago, IL, USA). The non-parametric independent 2-sample Mann-Whitney U test was used for comparisons of motor

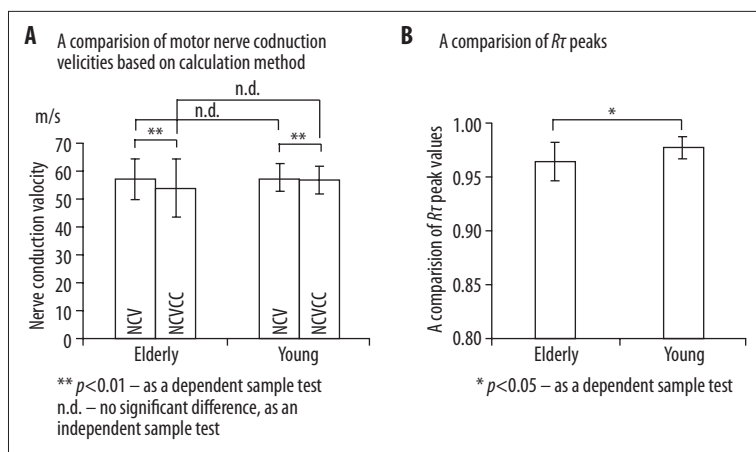


Figure 2. Comparison of calculated values for motor nerve conduction velocity in elderly and young. **(A)** In calculations of motor nerve conduction velocities for the same subject, whether elderly or young, *NCVCC* was significantly lower than *NCV* (** $p < 0.01$, as a dependent sample test). However, neither *NCV* nor *NCVCC* significantly differed between age groups. **(B)** R_{τ} peak (determined when *NCVCC* was calculated) was significantly higher in young as compared with elderly (* $p < 0.05$, as an independent sample test).

function and motor nerve function between the elderly and young subjects, and the non-parametric dependent 2-sample Wilcoxon test was used for comparisons between subjects. Pearson correlation coefficients and 2-tailed significance tests were used to estimate the correlation between the ratio of the 2 calculated values for motor nerve conduction velocity and the R_{τ} peak, which occurs when calculating *NCV2*.

Results

Motor function

In the overall comparison of subjects, although males had greater grip strength ($p < 0.01$), a faster TUG ($p < 0.05$) time, and a faster 5-m fastest walk time ($p < 0.01$) than females, there was no significant difference in 5-m normal walk time. As compared with the young subjects, elderly subjects had less grip strength ($p < 0.01$) and slower TUG ($p < 0.05$) and 5-m fastest walk times ($p < 0.01$). There was no significant difference in 5-m normal walk time (Table 1).

Motor nerve function

Four elderly individuals (2 males and 2 females) with a R_{τ} peak of less than 0.8 (determined when calculating *NCVCC*) were excluded from the analysis of motor nerve conduction velocity. The combined R_{τ} peak value of the remaining elderly and young subjects was 0.97 ± 0.016 (mean \pm SD) and ranged from 0.93 to 0.99. The motor nerve conduction velocity of the elderly and young subjects combined did not significantly differ by sex for either *NCV* or *NCVCC*. The *NCV* for elderly and young subjects was 58.1 ± 4.98 m/s and 55.7 ± 8.04 m/s, respectively, and the *NCVCC* was 57.1 ± 4.84 m/s and 53.5 ± 9.82 m/s, respectively; neither variable significantly differed between groups (Figure 2A). However, when comparing the results of the calculation methods among elderly and young subjects, *NCVCC* (as determined by the correlation coefficient) was significantly

less than *NCV* ($p < 0.01$). A significantly smaller R_{τ} peak was seen in the elderly group as compared with the young group ($p < 0.05$, Figure 2B) for *NCVCC*. A significant, slightly negative, correlation was observed between *DNCV* and R_{τ} peak among elderly and young subjects combined (Figure 3A). In addition, there was a significantly negative correlation ($r = -0.63$, $p < 0.01$) among elderly subjects, but no correlation among younger subjects (Figure 3B, 3C).

Discussion

Although the calculated values were similar among elderly and young persons for motor nerve conduction velocity on evoked EMG, age-related changes in nerve function were shown by a comparatively simple analysis method based on the shape of the CMAP, as detailed below.

Motor function of elderly subjects

The elderly subjects in this study were members of a municipal club and willingly volunteered for this research. Although measures of movements that require maximum muscle strength (including grip strength, standing from a seated position measured in the TUG test, and fastest walking time) were lower in the elderly group than in the younger group, there was no significant difference between age groups in movements required for daily living, such as the 5-m normal walk. Furthermore, every elderly subject met the BESTest (balance evaluation systems test) standard of < 11 s for the TUG (Table 1) [5]. Although sex differences were noted, the results showed no age-related decline in normal walking speed. The mean values for each physical activity were ranked according to the 5-level evaluation criteria of the “appraisal standards for functional measures in independent elderly people” (mid-point, level 3). Mean grip strength, which reflects upper limb motor function, was ranked at level 4 in both males and females (males: < 33 kg, females < 21 kg). TUG, 5-m normal walk, and 5-m fastest walk

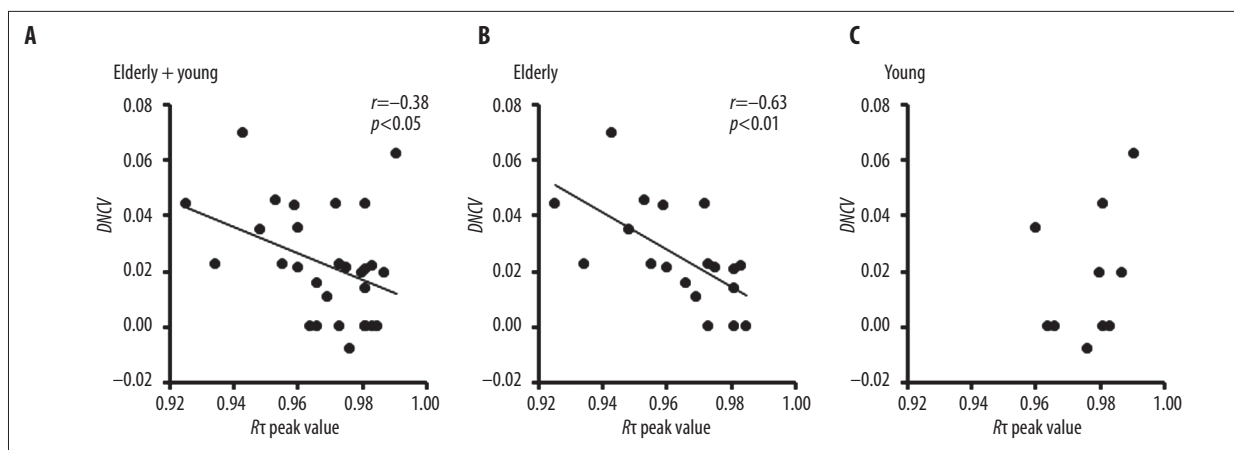


Figure 3. Correlation of *DMCV* and R_t peak. (A) A significant, slightly negative correlation was seen when young and old subjects were combined. (B) Among elderly subjects, a significant negative correlation was observed. (C) There was no correlation among young subjects ($r=0.33$, $p=0.35$).

reflect lower limb motor function and were also ranked at level 4 or higher. These above-average results for elderly motor function may be the direct result of regular physical activity in the municipal club.

Motor nerve function of elderly

Physiological degeneration of the myelin sheath accompanying the aging process causes a slight reduction of nerve conduction velocity. Studies of individuals in their 20s to 90s show maintenance of muscle mass even as age advances, and although some individuals suddenly decline during old age, nerve conduction velocity decreases in a slow, linear fashion [3]. The elderly participants in this study had an extremely low *NCV* (mean, 2.4 m/s), as compared with the young participants, and there was no significant difference between age groups. Furthermore, the elderly and young subjects did not obviously differ in motor nerve function, using the standard nerve conduction velocity obtained using equation (1). Although the lowest *NCV* among the 24 elderly subjects was 39.3 m/s, this value was excluded from analysis because the R_t peak was low (0.75). Among the remaining elderly subjects, the lowest individual value was 47.1 m/s, which is within the normal range, and is 94.2% of the lowest value observed in the young group (50 m/s). The motor nerve function of the elderly participants was examined using the ulnar nerve of the upper limbs. The grip strength, reflecting the function of the upper limbs, was high, with the lower limbs showing an equally high level of function. We believe that the present findings are representative of motor nerve function in healthy elderly individuals.

The standard motor nerve conduction velocity of *NCV*, the conduction velocity found using equation (1), is calculated on the basis of the latency time difference between the administration of the stimulus until the start of the action potential,

and reflects the fastest motor unit among compound action potentials [18]. In addition to this method, we also calculated nerve conduction velocity using a method that examines time difference from the cross-correlation of the various waves of the overall action potential waveform (*NCVCC*). Using this method, many motor unit components (ie, not just the fastest motor unit) can be compared. Therefore, as a measure of nerve conduction velocity, *NCVCC*, is considered to be significantly lower than *NCV*.

Although we calculated *NCVCC*, there was no significant difference in this variable between the healthy elderly and young subjects in this study. However, R_t peak, which was observed while calculating *NCVCC*, was significantly lower in elderly subjects. This result was obtained after removing data on the elderly individuals who had extremely low R_t peak. In a comparison of the evoked EMG values recorded from proximal and distal stimuli, the waveforms for elderly and young differed. The cross-correlations in this study were the normalized calculated wave, which removed amplitude differences between waves. Attenuation while maintaining the waveform was not reflected in R_t . CMAP amplitude is correlated not only with conduction blocks and aging, but also with height and body mass index [4]. Therefore, the effects of amplitudes were not analyzed in this study.

Abnormal changes to the nerve conduction waveform are caused by temporal dispersion or lack of conduction in a portion of motor units [19–21]. Conduction blocks may be caused by neural stenosis or demyelinating diseases, which are also accompanied by a decline in nerve conduction velocity. A correlation between a decline in muscle mass and pathological reductions in nerve conduction velocities innervating those muscles has also been reported [22]. Nerve conduction velocities also decline with long-term bed rest [23]. A variety of factors

are believed to contribute to reduced nerve conduction velocities associated with regular aging, including shortening of internodal length, focal demyelination, and axonal membranes [24–26]. Such changes cannot be evaluated using regular nerve function diagnostics. Changes in the nerve function of healthy elderly individuals vary depending on motor units. Even if a clear decline was evident in a portion of muscle fibers, *NCV* (which compares only the fastest motor nerves) would probably not show a change. However, if a decline occurs in a portion of motor nerves, *CMAP* waveforms should change when altering the stimulus site. For physically weak elderly individuals, even if a large decline was not observed using *NCV* (the standard method of calculating motor nerve conduction velocity), a comparison of overall waveforms using *NCVCC* can further reveal decline, as the difference between *NCV* and *NCVCC* would potentially widen. The scatter graphs in Figure 3 show a negative correlation between *DNCV* and a decline in R_f peak only in elderly subjects and thus support this hypothesis. These findings suggest that decline occurs in a portion of motor nerves even in physically strong elderly; therefore, elderly individuals with lower physical strength would probably show a much clearer trend. These results highlight the need to examine whether fast and slow components of the motor nerve conduction velocities of motor units shorten due to exercise. Furthermore, our findings suggest that it is possible to increase active motor function in addition to maintaining and improving motor nerve function.

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Conclusions

Even when motor nerve conduction velocities are normal, the distribution of the conduction velocities of motor units spreads with advancing age. By using cross-correlation of evoked EMG waves in conjunction with normal motor nerve conduction velocities to calculate motor nerve conduction velocity, the differences between these calculated values can be examined. By analyzing correlation coefficients, *CMAP* can provide more detailed information on changes occurring in motor nerve function in elderly persons.

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