anesthesia. If the afferent signals from the ankle joint affect the detection of passive movement, SLR and MLR activities of peripheral muscles would be influenced when the feet are perturbed during static standing. Accordingly, we have to consider whether the SLR and MLR activities of peripheral muscles are affected by decreased afferent signals from the ankle joint under unstable conditions.

We also have to consider that the supraspinal center affects stimulation of α-motoneurons of peripheral muscles when a person stands. The amplitude of MLR in leg muscles is sensitive to whether or not the subject can predict the postural task and whether the posture of the standing subject is stabilized or not[10, 11]. When a standing subject's balance is perturbed and the subject unable to predict the postural task, MLR activity of the leg muscles significantly increases compared to stable standing with predictable conditions for the postural task[12]. It has been concluded that monoaminergic brain stem centers selectively modulate the stimulation of the interneuronal pathways through group II afferents from homonymous spindle secondaries. However, it is not clear whether MLR activity of the peripheral muscles are affected by modulation from monoaminergic brain stem centers, if presynaptic or disynaptic inhibitions occur in afferent fibers connecting with the ankle joints during ankle vibration.

To cause hypoesthesia, mechanical vibrations were applied to Sol and malleolus of the subjects[13–15]. Vibration applied to peripheral leg muscles causes presynaptic inhibition of Ia and group II afferent fibers, and then stimulates the α-motoneurons of homonymous muscles via a decrease in interneuron numbers[16, 17]. In contrast, vibration applied to the malleolus raises the activation thresholds of the ankle mechanoreceptors making it harder to stimulate the receptors because of the receptors' raised threshold[18]. Information on the level of the vibration frequency used in several studies was helpful for our research. The vibration frequency which effectively raises the thresholds of muscle spindles and mechanoreceptors is approximately 100 Hz[14, 19, 20].

Therefore, we examined whether vibration near 100 Hz of the Sol and ankle joint affects Sol SLR and MLR activities during platform movements. We also examined whether monoaminergic brain stem centers modulate Sol MLR activity when vibration is applied to the Sol and ankle joint.

SUBJECTS AND METHODS

Ten healthy male subjects (aged 23–35 years, with a mean age of 27.9 years of age) participated in the experiments. The subjects gave their informed consent and the study conformed to the Declaration of Helsinki. The current research began after approval was obtained from the ethical committee of the Health Science Center of Kyushu University.

The subjects were asked to stand with their eyes closed, arms by their side with both feet on a movable platform (Equi-test version 8.1, NeuroCom Inc. USA). The center of mass (COM) of the subject was observed on the anterior-posterior and medial-lateral axes on a computer screen. The dot point, which indicates the COM of the subject, was observed before the platform perturbation. The COM was placed at the intersection point of the coordinate axes by the tester. The feet were grounded and the subject's height on the platform was taken into account. The movement of the platform was a backward displacement, which induces stretch and consequent reflex responses in the Sol muscle. Table 1 shows the amplitude of the movement of the platform. One series of measurements included 18–21 trials and the time interval between each trial within a series varied randomly from 1.5 to 2.5 seconds.

Table 1. Platform displacement amplitude

Intensity	Duration time (ms)	Perturbation (cm)
large	400	4.6–6.0

The distance of platform movement was related to the height of the subject

The vibrators contained a DC motor with an eccentric the embedded in rectangular plastic case, 3 cm wide, 6 cm long and approximately 2 cm high (MCL-1701, Alinco Inc. Japan). Vibrators (92 Hz) were bilaterally fixed to the Achilles' tendons (Sol vibration condition, SV) and to the lateral and medial malleolus (malleolus vibration condition, MV) by elastic bands. The vibrators were turned off in the control condition (without vibration). In the SV and MV conditions, vibration was applied for one minute before the beginning of platform movement and was continued for 18 to 21 trials (about six minutes respectively). The vibrator produced a peak-to-peak force of about 4 N (4.13 ± 0.12 N), as measured by the strain gauge (EM-555, Noraxon Inc. USA) that was placed between the skin and the vibrator[14].

Three trials on the platform comprised a single unit. The subject executed a single unit 6 or 7 times (18–21 trials) without rest. In each unit, the interval between each trial was randomly set to vary from 1.5 to 2.5 seconds. Each condition was examined randomly. Noda et al.[13] reported that 5 minutes of conditioning vibration applied to the malleolus of normal subjects increased the vibratory perception threshold at 10, 60 and 120 seconds, but not at 5 minutes. Therefore, a rest period of 5 minutes was provided between the measurement series during which the subjects adopted a comfortable sitting position. Sol muscle EMG responses to backward platform movement under each of three conditions were collected for each subject.

EMGs were recorded using surface electrodes. The distance between the surface electrodes was approximately 2 cm. The electrodes were positioned on the skin 3 cm below the bottom of the medial head of the gastrocnemii to record the EMG activity of Sol on the right leg. The EMG signal was amplified (10,000×) and band-pass filtered from 10 to 500 Hz. The analog signal was digitally converted at a sampling rate of 1 kHz, and the onset signal of platform movement was synchronously recorded on a personal computer. All of the identified EMG wave shapes were rectified. The acquisition period was 350 ms, with the platform movement starting at 100 ms from the onset.

All Sol responses of EMG were smoothed (time constant 10 ms), and the onsets of SLR and MLR in Sol were defined as when the EMG signal rose above 2 SDs of the mean value of the background EMG activity before the beginning of

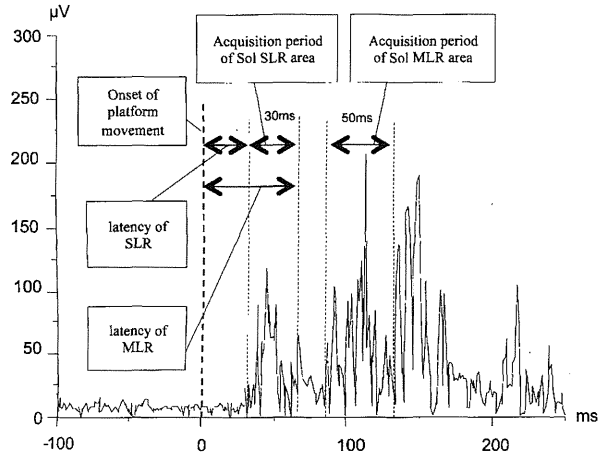

Fig. 1. Samples of measurement items of rectified EMGs of Sol This panel shows a representative sample of the rectified Sol EMG during the backward platform movement. The measurement items were the latencies of Sol SLR and MLR onsets, the SLR area (%MIVC) and MLR area (%MIVC).

platform movement. The responses in the stretched Sol were classified as SLR or MLR when their onset latencies were shorter or longer than 60 ms [3, 14], respectively. The SLR and MLR areas were calculated using the average of the rectified and filtered (time constant 1 ms) EMG traces. In our pilot study, the acquisition periods of rectified and integrated SLR and MLR EMG areas in Sol were respectively determined at 30 ms and 50 ms by smoothed EMG (unpublished). The areas were measured in a time window of 30 ms for Sol SLR and 50 ms for Sol MLR from the onset of the responses[14] (Fig. 1). Time windows of the same acquisition periods were then used to measure the areas of the responses in each single trial under each of the three conditions. Sol SLR and MLR EMG responses of each subject were normalized with respect to the EMG activity of an equivalent duration recorded during maximal isometric voluntary contraction (MIVC) of the Sol muscles to compare the findings across all subjects. The epoch of acquisition of the EMG MIVC signal began 2 s after MIVC onset and lasted for 500 ms.

A one-way (3 group × 2 responses) analysis of variance (ANOVA) was performed for the three conditions to compare the latencies of Sol SLR and MLR onsets. Analysis of covariance (ANCOVA) was used to assess the effects of Sol MLR EMG area with respect to SLR EMG area and each of the three conditions. The three conditions were covariance (independent variables) and Sol MLR EMG area was a dependent variable. The Bonferroni/Dunn post hoc test was employed when the results of ANOVA were significant. A linear regression analysis was used to evaluate the trials under each of the three conditions to characterize the relationship of the Sol SLR and MLR areas. The regression coefficient and intercepts of the three conditions were evaluated with the Bonferroni/Dunn test (the SLR area was a covariate). P values of less than 0.05 were considered statistically significant.

RESULTS

Table 2 shows the overall average of onset latencies of Sol SLR and MLR in response to the platform backward movement under the three conditions. ANOVA revealed the vibration had a significant effect on the latencies of Sol SLR ($F=93.879$; d.f.$=2, 561$; $p<0.0001$) and MLR ($F=36.957$; d.f.$=2, 561$; $p<0.0001$). Vibration caused a significant delay in Sol SLR of approximately 2.5 ms under the SV condition and 2 ms under the MV condition compared to the control value (post hoc test, $p<0.01$ and $p<0.01$, respectively). Vibration induced a significant delay in Sol MLR of 6 ms under the SV condition and of approximately 3 ms under the MV condition in comparison to the control value (post hoc test, $p<0.01$ and $p<0.01$, respectively).

From the analyses of the effects of Sol MLR EMG area with respect to SLR EMG area among the three conditions (ANCOVA), Sol MLR EMG area was affected by Sol SLR EMG area ($F=300.323$; d.f.$=1, 561$; $p<0.0001$) and conditions ($F=3.154$; d.f.$=2, 561$; $p<0.05$). There was not an interaction between covariate of the conditions and independent variable of Sol SLR areas (Table 3).

A slightly positive relationship was found between the Sol MLR and SLR areas under the control condition ($y=1.896+0.675x$; $p<0.0001$). A more positive relationship was found between the two areas under SV ($y=1.605+0.809x$; $p<0.0001$). The regression line under the MV condition was moderately positive between the two areas, but the coefficient of regression was slightly lower than that under the control condition ($y=2.254+0.641x$; $p<0.0001$). The coefficients of regressions were not different between the SV and MV conditions. The intercept under the MV condition rose significantly more than under the SV condition (Bonferroni/Dunn test; $p<0.01$). In Table 3, the intercept of the regression line was lower under the SV condition than under the MV condition.

DISCUSSION

Both Sol SLR and MLR latencies under the SV condition increased. There is accumulating evidence that Ia and group II afferent fibers from Sol muscle spindles show presynaptic inhibition when a vibration frequency of nearly 100 Hz is applied[13, 14, 21–23]. This evidence will help us to have a thorough understanding of the delay mechanism of Sol SLR and MLR onsets. Delays of Sol SLR and MLR onset might correspond to the delay of temporal summation of α-motoneurons due to presynaptic inhibition of Ia and group II afferent fibers.

The onset latency of Sol SLR and MLR was also extended under the MV condition. It is documented that afferent fibers from the ankle joints have disynaptic connections to α-motoneurons of the quadriceps femoris muscles[24]. From these delays of Sol SLR and MLR latencies under the MV, the afferents from the ankle joints are also assumed to constitute the pathways to α-motoneurons of Sol. The afferent fibers from several mechanoreceptors of the ankle joints are group I and II afferent fibers[25]. Thus, excessive afferent signals from the ankle joint under vibration seem to

Table 2. One-way analysis of variance of differences among the control, Sol vibration and malleolus vibration conditions of the onsets of Sol SLR and MLR

	Condition		
	Control	Sol vibration (SV)	Malleolus vibration (MV)
Onset of Sol SLR (ms)	38.1 ± 0.2	44.6 ± 0.4§§	41.2 ± 0.4** ††
Onset of Sol MLR (ms)	68.5 ± 0.6	74.6 ± 0.4§§	71.6 ± 0.5** ††

§§ indicates significant difference ($p<0.01$) between control and SV conditions in post hoc test (The Bonferroni/Dunn test). ** indicates significant difference ($p<0.01$) between control and MV conditions in post hoc test (The Bonferroni/Dunn test). †† indicates significant difference ($p<0.01$) between SV and MV conditions in post hoc test (The Bonferroni/Dunn test). SLR: short latency reflex, MLR: medium latency reflex. Each value is mean ± S.E.

Table 3. Coefficient and intercept values of the linear regression models of $\log_e$ Sol MLR area (dependent variable), $\log_e$ Sol SLR area (independent variable), and condition (covariance) with analysis of covariance

	Condition (Covariance)		
	Control	Sol vibration (SV)	Malleolus vibration (MV)
Regression Coefficient	0.68**	0.81**	0.64**
Intercept	1.90**	1.61**	2.25** ††

Log_e MLR area, $\log_e$ SLR area and condition are the dependent variable, independent variable and covariance, respectively. **: significance of regression coefficient and intercept ($p<0.01$). ††: significant difference ($p<0.01$) of intercepts between SV and MV conditions in post hoc test (The Bonferroni/Dunn test)

inhibit interneurons (disynaptic inhibition) via group I and II afferent fibers from the ankle joint. These clear delays in Sol SLR and MLR onsets under MV support the notion that disynaptic inhibition of interneurons connected to group I and II afferent fibers from the ankle joint extend the time required temporal summation of Sol α-motoneurons.

In the regression analyses of the Sol MLR and SLR areas under the three conditions, the coefficients regression of the SV and MV conditions were not different. In contrast, the intercept under the MV conditions was greater than under the SV condition. Therefore, this result indicates that Sol MLR activity increases when vibration is applied to the ankle joint but decreases when vibration is applied to the homonymous muscles. It is documented that the Sol SLR and MLR areas with toe-up rotation, during Achilles tendon vibration of 90 Hz, of standing subjects exhibited significant decreases in comparison to the absence of vibration[14]. This finding is explained by the presynaptic inhibition of Ia and group II afferents from muscle spindles which are being vibrated[16, 21–23]. Sol MLR area under the SV condition is consistent with the results of previous studies in which vibration was applied to Sol. Therefore, we think that vibration applied to Sol α-motoneurons decreased because of presynaptic inhibition of Ia and group II afferent fibers induced by Sol vibration.

However, the intercept of the regression line was higher under the MV condition than under the SV condition. This result does not support the theory of disynaptic inhibition alone, because the Sol MLR area during the MV condition increased. When subjects support themselves by holding onto a stable frame, then the same foot rotation elicits responses of a smaller magnitude, of less than 20% on the average of the control value [23, 26]. This finding led to the conclusion that monoaminergic brain stem centers selectively modulate the stimulation of the interneuronal pathways responsible for the transmission of group II input[19]. In our pilot study, the latencies and amplitudes of Sol SLR and MLR were respectively delayed and decreased by evoked-potentials (MEB-9404, Nihon-Kohden Inc., Japan), when vibration was applied to the malleolus of stable standing subjects, compared to the control condition (unpublished). That is, monoaminergic brain stem centers may compensatorily excite the interneuronal pathway via group I and II afferents from the ankle joint while disynaptic inhibition took place during ankle vibration under unstable standing conditions. This compensatory effect of monoaminergic brainstem centers was corroborated by the results of another of our studies, which demonstrated that the SLR and MLR areas of plantae muscles decreased under the same MV condition[27]. The monoaminergic brain stem centers may predominantly modulate reflexive Sol activity when standing conditions are unstable, and afferent signals from the ankle joint would be inhibited because plantae muscle activity is strongly inhibited by excessive afferent signals from the ankle joint during vibration. Moreover, Sol activity is directly related to the intensity of the ground reaction force and the displacement of the center of pressure[28, 29].

We should point out that compensatory modulation from the supraspinal centers had little effect on the Sol MLR area under the SV condition similar to the MV condition. This

discrepancy might be caused by the character of the perturbation. The perturbation used in our present study was the backward perturbation of a platform. It is known that the decrement of afferent signals from the ankle increases error in passive position sense of the ankle joint, but does not affect stability during static standing because of compensatory inputs from muscle spindles as a result of the anesthetsia of the ankle joint[9]. The afferent signals from Sol muscle spindles would contribute to stability during static standing, however the afferent signals from the ankle joint rather than from Sol muscle spindles might contribute to reflexive Sol activity during passive movement of the feet. Therefore, supraspinal centers might not participate in modulating the stimulation of interneuronal pathways involved in Ia and group II afferent fibers from Sol muscle spindles under SV, even if the afferent fibers from Sol muscle spindles resulted in presynaptic inhibition during Achilles' tendon vibration.

Another point we must notice is the composition type and motor units of the Sol muscle fibers. Previous investigations have demonstrated that the Sol fibers consist of 81% type I, 16% type IIa and 0% type IIb fibers[30]. Moreover, it has been proposed that α-motoneurons that innervate fiber types I and II mainly have connections with group II and group I afferent fibers in the peripheral nerves[31]. Since the fiber type of Sol is mostly type I fiber, group II afferent fibers from the ankle joint and other group II afferent fibers from Sol muscle spindles that mediate Sol MLR activity might form concentrative synaptic connections with Sol α-motoneurons innervating type I fibers. Therefore, monoaminergic brain stem centers might provide compensatory stimulus to the α-motoneurons of Sol, even though the Sol MLR area would be expected to decrease with disynaptic inhibition of group II afferents under MV.

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Normative Data for the Montreal Cognitive Assessment in a Japanese Community-Dwelling Older Population

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Key Words
Cognitive decline · Cognitive screening · Dementia · Cross-sectional study · Community-based study · Elderly · Mild cognitive impairment

Abstract
Background: Although the Montreal Cognitive Assessment (MoCA) is acknowledged as a promising neuropsychological tool, its normative data for older populations have not been established yet. The purpose of this study was to provide normative data for the MoCA in Japanese community-dwelling older people. ***Methods:*** In a Japanese town, 1,977 participants aged 65 years or older (mean age 73.6 years; male 41.3%) completed MoCA tests. After descriptive and regression analyses, normative data were developed for MoCA scores in the population. ***Results:*** The mean MoCA score observed (21.8 points) was lower than that for normal controls (27.4 points) in the original validation study of the MoCA. Additionally, 82.6% of MoCA scores fell below the standard cutoff of 26 points for detecting mild cognitive impairment (MCI). The regression analysis showed that higher age and fewer years of formal education were associated with lower MoCA scores ($p < 0.001$). Normative data for MoCA scores were presented with respect to age and education. ***Conclusion:*** This study provided normative data for the MoCA in a Japanese community-dwelling older population. This research also suggests that conventional use of the MoCA as a screening tool for MCI might be problematic in cultures different from that in which the cutoff was developed.

Introduction

Mild cognitive impairment (MCI) represents an intermediate clinical state between normal cognitive aging and Alzheimer's disease or other types of dementia [1]. Although it is not always the case, MCI has been reported to often develop into either Alzheimer's disease or other forms of dementia and, therefore, recognized as a high-risk state for dementia development [2]. In recent discussions, community-based screening of MCI is considered one of the crucial steps to enable wide-reaching interventions for preventing or slowing the onset of dementia [3].

Montreal Cognitive Assessment (MoCA) is a brief neuropsychological tool designed for screening MCI in community health care [4] and is acknowledged as a promising instrument worldwide [5–7]. Given the need for ethnic-specific versions of neuropsychological tests [8, 9], 38 versions of the MoCA are currently developed in 31 languages (www.mocatest.org). MoCA has also

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been reported to have higher sensitivity to a subtle cognitive decline than conventional tools such as the Mini-Mental State Examination [4, 10, 11]. To date, two cohort studies reported normative MoCA data in population-based samples including a multiethnic US population [12] and a Portuguese population [13]. Both studies, however, were conducted with subjects of a wide age range, and thus, the sample sizes were scarce for the older age groups.

Because older people are the primary subjects of MCI screening and subsequent interventions, their scoring characteristics on the MoCA should be examined and demonstrated with a larger sample size. This is an urgent matter, especially for a Japanese society undergoing the world's fastest aging with the highest life expectancy. Therefore, the aim of the present study was to provide normative MoCA data specific to community-dwelling older people in a Japanese town.

Materials and Methods

Participants

The present study involved analysis of data from the baseline phase of the Sasaguri Genkimon Study (SGS) conducted from May to August 2011. The SGS is an ongoing community-based prospective cohort study in a Japanese local town, Sasaguri, aiming to explore modifiable lifestyle factors causing older people to require nursing care. Subjects of the baseline study (SGS-1) were all residents of the town who were aged 65 years or older and not certified as individuals requiring nursing care by the town in January 2011 (n = 4,979). Sixty-six subjects were excluded due to being dead or moving out by the onset of the study. A set of study information sheets and a questionnaire were mailed to all remaining subjects (n = 4,913), and 2,629 individuals, hereafter referred to as the participants of the SGS-1, responded to the mail by (1) visiting a community center to submit the questionnaire and undergo multiple physical and cognitive tests in one of 31 group-testing sessions of the SGS-1, (2) contacting study coordinators to set up an appointment for an individual home-testing session or (3) visiting the city office to submit the questionnaire (recruitment rate: 53.5%). Of these, 2,129 individuals took part in the MoCA tests. After the testing, we excluded 32 individuals who were unable to complete the MoCA properly, 12 individuals with missing information about their years of formal education, and 108 individuals with self-reported medical histories of stroke, depression, Parkinson's disease and dementia. Accordingly, data from 1,977 participants (75.2% of the total participants of the SGS-1) were involved in the present study.

Standard Protocol Approvals, Registrations and Patient Consents

All the participants provided written informed consent to participate in the present study. The study protocol and the informed consent form were approved by the Institutional Review Board of the Institute of Health Science, Kyushu University.

Measurements

We used the Japanese version of the MoCA for all measurements. The details of the Japanese version are described elsewhere [5]. Briefly, it was developed and validated by investigators, including the inventor of the original MoCA (Dr. Nasreddine). As in the original one [4], the Japanese version of the MoCA was designed as a 30-point screening instrument administered in about 10 min and consists of the following 12 cognitive tasks: a five-item delayed recall task (5 points), a clock-drawing task (3 points), a cube-copying task (1 point), a trail-making task (1 point), a phonemic fluency task (1 point), a two-item verbal abstraction task (2 points), a target-tapping task (1 point), a serial subtraction task (3 points), a two-item digits-reading task (2 points), a three-item naming task (3 points), a two-item sentence-repeating task (2 points) and a six-item temporal and locational orientation task (6 points). In the standard procedure of the original as well as the Japanese versions, 1 point is added to the total score of the cognitive tasks if an individual has 12 years or fewer of formal education, and a final total score falling below 26 points is judged to have probable MCI.

Procedures

All MoCA tests were administered to the participants by trained personnel as part of the group-testing and home-testing sessions of the SGS-1. After the testing, MoCA scores were independently evaluated by two authors (K.N. and T.H.) and double-checked between the two before being finally determined. The interevaluator reliability, shown as a percentage of agreement in the MoCA scores, was 93.3% in the initial evaluation. To demonstrate normative data in participants with a wide range of years of formal education, the preferred 1-point correction for education was not adopted.

Statistical Analyses

All statistical analyses were conducted using SAS version 9.2 (SAS Institute Inc., Cary, N.C., USA). The Wilcoxon rank-sum test and the χ^2 test were conducted to compare age and sex, respectively, between the participants of the present study and the rest of the subjects (n = 2,936). The Wilcoxon rank-sum test was also performed to assess the difference in years of formal education between the participants of the present study and the rest of the participants of the SGS-1 answering educational history in the questionnaire (n = 608). Descriptive statistics were calculated for MoCA scores and for scores of respective cognitive tasks. A multiple regression analysis was performed with the MoCA score as a dependent variable and age, sex and years of formal education as independent variables. Additionally, to visualize changes in MoCA scores, simple regression analyses were conducted between the MoCA score and age in three education levels ($\leq$9, 10–12, and $\geq$13 years of formal education). Subsequently, normative data for MoCA scores in the community-dwelling older population were developed with respect to age and education. Overlapping age categories of 65–75, 70–80, 75–85, and $\geq$80 years, accompanied by the aforementioned three education levels, were adopted in the normative data based on the rationale previously described for practical use of the normative data in community health care [12, 14]. A significance level was set at two-sided $\alpha = 0.05$.

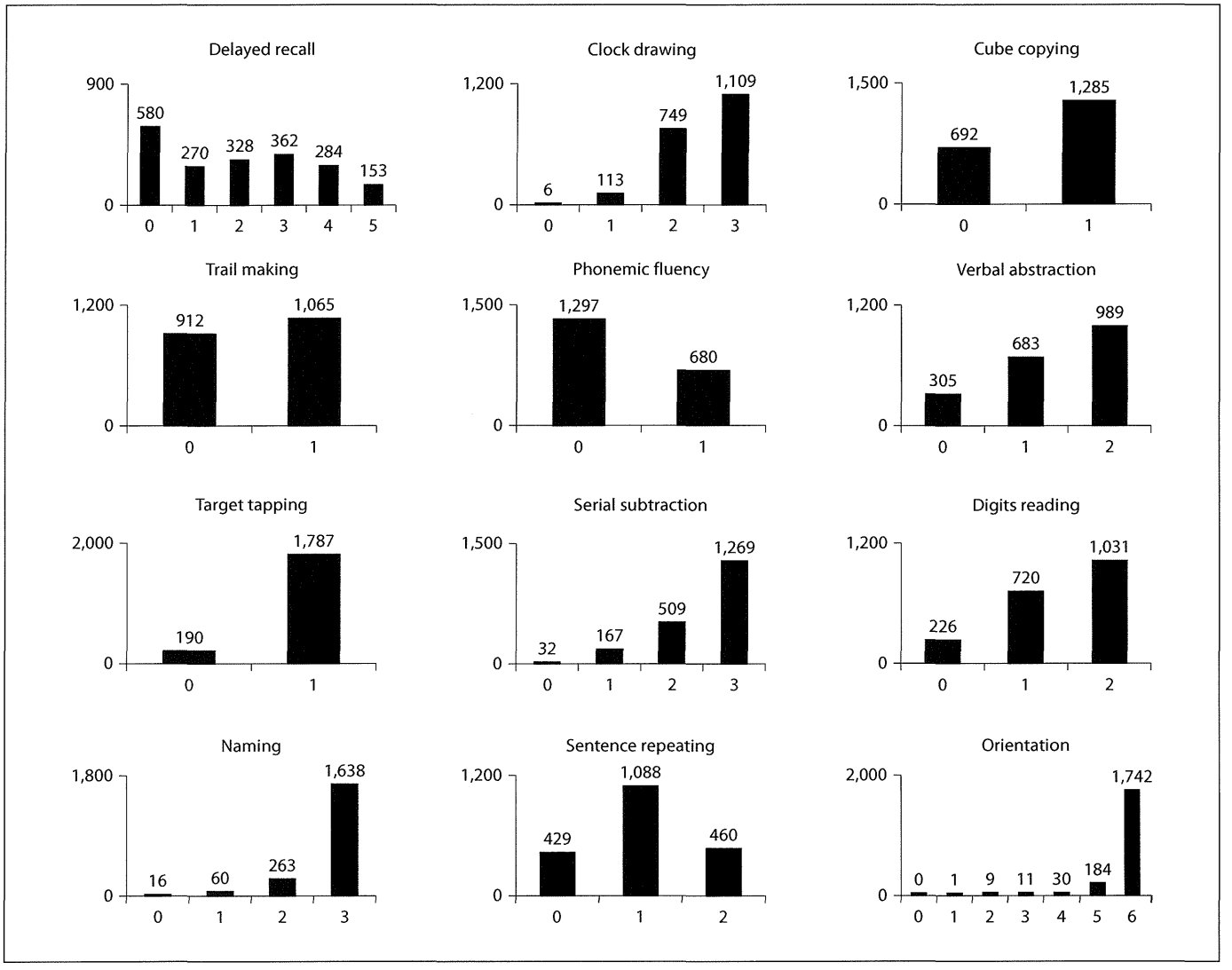

Fig. 1. Histograms of scores for respective cognitive tasks in MoCA. Each panel shows a histogram for one of the 16 cognitive tasks in the MoCA. Horizontal and longitudinal axes of each panel indicate points scored and frequency count for each point, respectively.

Results

The participants of the present study differed from the rest of the subjects in terms of sex (percentage of males, 41.3 vs. 45.3%; p = 0.008), but not in terms of age (median, 72 years for both groups; interquartile range, 68–78 years for both groups; p = 0.860). Also, the number of years of formal education was not different between the participants of the present study and the rest of the participants of the SGS-1 answering educational history in the questionnaire (median, 12 years for both groups; interquartile range, 9–12 years for both groups; p = 0.216). The mean age of the participants was 73.6 years (standard deviation, SD, 6.2; median, 72; range, 65–96) and the number of years of formal education was 11.0 years (SD, 2.5; median, 12; range, 2–23); 41.3% of the participants were male (n = 817). The mean MoCA score was 21.8 points (SD, 3.9; median, 22; range, 5–30), with 82.6% of scores falling below the preferred cutoff of 26 points for probable MCI. Histograms with scores of the respective cognitive tasks are summarized in figure 1.

In the multiple regression analysis, significant associations with the MoCA score were found for age (regression coefficient, –0.21; 95% confidence interval, CI, –0.23

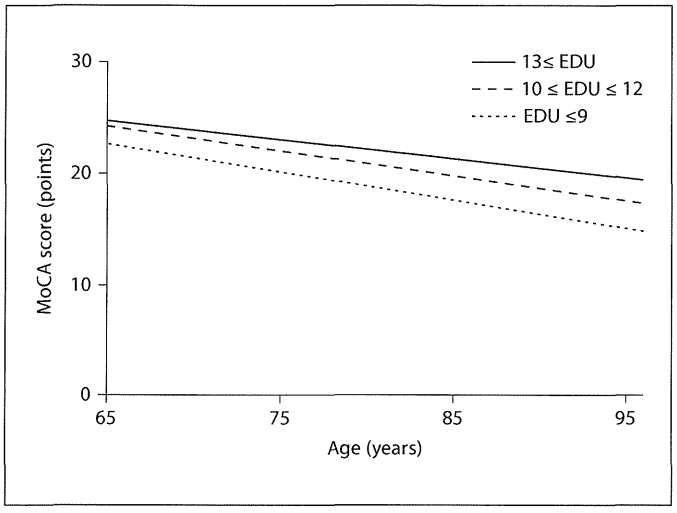

Fig. 2. Regression lines between age and MoCA scores in three education levels. EDU denotes years of formal education. Intercepts (at 65 years) and slopes for respective regression lines are as follows: 24.73 and −0.17 in 13 ≤ EDU; 24.30 and −0.22 in 10 ≤ EDU ≤ 12; 22.66 and −0.25 in EDU ≤9.

Table 1. Normative data for MoCA scores

	Education level			Total by age
	≤9 years	10–12 years	≥13 years	
Age category				
65–75 years	371	659	248	1,278
	21.4 ± 3.7	23.3 ± 3.1	24.0 ± 3.0	22.9 ± 3.4
	22 (9–29)	23 (14–30)	24 (13–30)	23 (9–30)
70–80 years	406	471	157	1,034
	20.2 ± 3.8	22.1 ± 3.4	23.2 ± 3.0	21.6 ± 3.7
	20 (6–29)	22 (12–30)	23 (13–29)	22 (6–30)
75–85 years	327	320	83	730
	19.2 ± 4.0	21.3 ± 3.4	22.6 ± 3.1	20.5 ± 3.9
	19 (5–28)	21 (12–29)	23 (16–29)	21 (5–29)
≥80 years	161	170	35	366
	18.0 ± 4.4	20.5 ± 3.5	22.1 ± 4.0	19.6 ± 4.2
	19 (5–28)	21 (8–29)	23 (12–29)	20 (5–29)
Total by education	692	964	321	1,977
	20.1 ± 4.1	22.5 ± 3.4	23.6 ± 3.2	21.8 ± 3.9
	20 (5–29)	23 (8–30)	24 (12–30)	22 (5–30)

Data are expressed as number, mean ± SD and median (with range in parentheses).

to −0.18; $p < 0.001$) and education (regression coefficient, 0.42; 95% CI, 0.36–0.49; $p < 0.001$) but not for sex (regression coefficient, 0.21; 95% CI, −0.10 to 0.52; $p = 0.186$). Figure 2 demonstrates the results of the simple regression analyses showing significant associations between the MoCA score and age in all three education levels ($p < 0.001$). Specifically, higher age was associated with lower MoCA scores in all the education levels. Finally, normative data for MoCA, specific to the community-dwelling older people, were determined with respect to the four age categories and three education levels (table 1).

Discussion

Population-based screening for MCI is recognized as a key step in establishing sound wide-reaching intervention programs for preventing or delaying older people from developing dementia [3]. Although the MoCA has great promise as a screening tool for MCI, knowledge regarding its scoring characteristics in population-based older samples has still been limited. To our knowledge, the present study was the first to demonstrate normative MoCA data specific to community-dwelling older people not only in Japanese society but worldwide. Reflecting the world's highest population aging rate in Japan, the normative data were formed with a relatively high proportion of old-old and oldest-old samples (table 1), which should be informative for other societies besides Japan. The present study also examined the associations of socio-demographic factors, including age, sex and years of formal education with MoCA scores in the older population.

In an attempt to develop normative data reflecting cognitively normal samples, we excluded individuals from the present analyses if they self-reported medical history of diseases contributing to or reflecting the development of clinical cognitive decline [2, 10, 15, 16]. There exists an argument that normative values should be representative and, therefore, should be developed from samples including both cognitively normal and abnormal individuals [17]. However, we made the exclusion based on the promise that the sensitivity of screening or detecting cognitively impaired individuals can be enhanced by comparing a patient's score to that of a reference group free of any clinical cognitive decline [18]. The exclusion of individuals requiring nursing care in the subject selection process may also be conducive to enhancing the sensitivity.

The mean MoCA score of 21.8 points observed in the present study was lower than that for the normal controls

(n = 90; mean, 27.4 points; SD, 2.2) and was indeed close to that for the patients with MCI (n = 94; mean, 22.1 points; SD, 3.1) in the original normative study performed by the development group of the MoCA [4]. These trends were unchanged even after the preferred 1-point correction of MoCA scores for formal education (mean, 22.7 points; SD, 3.8). Furthermore, more than three quarters of the scores (82.6% without the correction or 75.1% with the correction) fell below the preferred cutoff of 26 points for detecting MCI while the reported prevalence of MCI in older populations ranges from 15 to below 30% [19–23]. This percentage is still high even considering the potential inclusion of patients with undiagnosed dementia. Because multiple population-based studies have also observed MoCA scores comparable to the present one [12, 13, 24], this discrepancy may not be attributed to some administrative issues in the present study but to a low external validity of the cutoff score due to the limited number of samples and/or possible selection bias for the non-population-based samples in the original study [4]. Other possible causes of the discrepancy are some cultural and linguistic artifacts occurring in the translation process of the original MoCA into the Japanese version [8, 18]. Although the cross-cultural and cross-linguistic adaptations appear to be taken into account during the development process of the Japanese version [5], the validity of the adaptations was examined with a limited number of clinical-based subjects and, therefore, the possibility of cultural and linguistic artifacts in population-based use cannot be ruled out.

As observed in previous population-based studies with subjects in a wide age range [12, 13], the present results show significant associations of age and education with the MoCA scores in older samples. Specifically, MoCA scores were lower in participants with higher age and/or fewer years of formal education. In contrast, no association was found between sex and the MoCA score. The effects of age and education have been well documented for neuropsychological tests in population-based studies and have been taken into account with age- and education-specific norms when the obtained scores have been evaluated [17, 18]. Because both age and education are now recognized as risk factors of cognitive decline [25, 26] rather than just biasing factors of the tests, it can be misleading and problematic to count the effects by adjusting an obtained score for these variables and evaluate the adjusted score using a single cutoff [17, 27]. In the light of this discussion, the current MoCA procedure, comprising a 1-point adjustment for 12 or fewer years of formal education and a subsequent evaluation with a single cutoff of 25/26, may not be the best for screening MCI in population-based samples.

Taken together, it is considered reasonable to assume that the current MoCA procedure is somewhat premature for MCI screening in community-dwelling older people. However, because we didn't employ a clinical diagnosis of MCI in the research design, the present study is unable to further propose any alternative criteria for population-based MCI screening. Instead, at this stage, the normative data demonstrated in the present study can allow clinicians and researchers to detect individuals with abnormal cognitive decline from the community-dwelling older samples while taking into account the influence of age and education. For example, if a 75-year-old patient with 9 years of formal education scored 12 points on the MoCA test, his or her personal physician can appreciate that the score was lower than the mean minus 2 × SD [i.e. 20.2 – (2 × 3.8) = 12.6] for the age- and education-matched normal group and can suspect the patient's clinical cognitive decline. Similarly, the normative data may be useful for professionals when monitoring subtle cognitive change within a patient in longitudinal observations. It should be noted here that the definition of normal or abnormal needs to be carefully made in practical use, depending on the context and circumstances in which the MoCA test is administered.

Our report has some limitations which are worth noting here. First, the sample of the present study was affected to some extent by the nonresponse, withdrawal and exclusion of originally designated subjects. Specifically, the participants of the present study differed from the rest of the subjects in terms of sex distribution. However, we believe the influence of this discrepancy on the present results was not considerable because the regression analysis showed no association between sex and the MoCA score. Second, because the present study was performed in a single Japanese town, generalizability of the results is somewhat limited. Nevertheless, the present normative data can be considered applicable to other places in Japan because ethnicity and educational system are almost homogeneous across Japan. Finally, in the normative data, some strata were formed with relatively small numbers of samples and, thus, are probably less reliable in terms of age-education relationships.

Associations of MoCA scores with other socio-demographic factors, such as ethnicity, culture, language, financial security and family configuration, remain to be explored by future investigations in order to generalize the findings of this research. Obtaining these types of re-

search findings might be essential before establishing the cutoff for population-based MCI screening. In parallel with exploring the future use of the MoCA as a population-based MCI screening tool, we are going to follow the present participants in prospective observations of the SGS to determine the ability of the test to predict the future onset of dementia in the community-dwelling older population.

Conclusion

In summary, the present research reported normative data for MoCA scores derived from a relatively large-scale community-dwelling older population in Japan and proposed practical applications of the normative data in community health care. This research also suggests that conventional use of the MoCA as a screening tool for MCI might be problematic in cultures different from that in which the cutoff was developed.

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Disclosure Statement

The authors declare that there are no conflicts of interest.

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