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Cognitive function and falling among older adults with mild cognitive impairment and slow gait

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Aim: To examine the association of the combination of slow gait and mild cognitive impairment (MCI) with cognitive function and falling in community-dwelling older people.

Methods: Participants were selected from the Obu Study of Health Promotion for the Elderly ($n = 3400$), and underwent gait examination and a battery of neuropsychological examinations, including the Mini-Mental State Examination and the National Center for Geriatrics and Gerontology Functional Assessment Tool (tablet version of Trail Making Test Part A and B, Symbol Digit Substitution Task, Figure selection task, Word memory and Story memory), and were interviewed with a series of questionnaires including medical history, physical activity, geriatric depression scale and fall history.

Results: Participants were classified into control ($n = 2281$), slow gait speed (SG; $n = 278$), MCI ($n = 673$) and MCI with SG (MCI+SG; $n = 168$) groups. All cognitive functions were significantly affected by the group factor, even adjusting for participant characteristics as covariates ($P < 0.001$). Post-hoc analysis showed that the control group had better performance than the other groups, and the MCI+SG group had worse performance than the other groups in all cognitive functions (all $P < 0.05$). In multiple logistic regression analysis, SG and MCI were independently associated with falling (all $P < 0.05$), and MCI+SG had a higher odds ratio for falling (adjusted OR 1.99, 95% CI 1.08–3.65).

Conclusions: Our findings support the idea that slow gait and MCI were related, and concurrently associated with falling. Motor function among MCI subjects should be focused on to assess profile risks. **Geriatr Gerontol Int 2015; 15: 1073–1078.**

Keywords: cognition, elderly, gait, mild cognitive impairment, neuropsychological assessment.

Introduction

Gait and cognitive impairment are common health problems among older adults. Slow gait speed is one of the components of frailty associated with falling, disability and several adverse health outcomes,[1] and even with survival,[2] whereas cognitive impairment – particularly mild cognitive impairment (MCI) – is considered to have a higher risk of conversion to Alzheimer's disease (AD), and most types of dementia.[3] Gait slowing is linked to the worsening of cognitive impairment and precedes even MCI, let alone overt dementia.[4,5] Additionally, gait and cognitive impairment are also prominent independent risk factors for falls.[6]

Subjects with MCI have a higher risk of conversion to dementia than the general older population,[3] whereas slow gait speed is a risk factor for cognitive decline,[7] and precedes MCI.[5] The combination of slow gait with cognitive impairment or complaints predicts a higher risk for dementia compared with healthy subjects or those without this combination.[8,9] In fact, slow gait speed followed age-related changes in the brain, including brain atrophy,[10] white matter hyperintensities[10,11] and was even associated with the accumulation of brain pathology at autopsy.[12] However, whether MCI with slow gait associates with cognitive function, compared with MCI with robust gait, is not fully understood.

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In addition, the combined effects of slow gait and MCI on falling are not clear. Both gait and cognitive impairment independently increased the risk of falling.[6,13] The status of MCI itself was also one of the risks for falling examined in a prospective study,[14] although there was some debate about the relationship between MCI and falling.[15,16] Montero-Odasso *et al.* suggested that both cognitive and gait impairment increased falling risk in a concurrent manner.[17] However, the association of falling with the combination of MCI and slow gait speed has not been investigated in a large cohort study with an adequate sample.

The present study aimed to examine the effects of slow gait speed and MCI on cognitive function and falling. Our hypothesis was that MCI patients with slow gait speed had decreased cognitive function and associated falls, compared with subjects with only slow gait or MCI, respectively. In addition, there is still some debate about the association of slow gait speed with cognitive function in a specific domain or with comprehensive cognitive decline.[7,18] Thus, we carried out a large cross-sectional study and neuropsychological assessments in multiple domains to assess cognitive function comprehensively.

Methods

Participants

Subjects eligible for this study were participants of a population-based cohort study, the "Obu Study of Health Promotion for the Elderly" (OSHPE), carried out from August 2011 to February 2012. A total of 5104 individuals participated in the OSHPE.[19] In the current study, we included participants who were independent with basic activities of daily living (ADL; confirmed by interview and not certified by long-term care insurance), and excluded participants who had a history of cerebrovascular disease, Parkinson's disease, depression or dementia (n = 4540). Then, participants who scored 23 or lower on the Mini-Mental State Examination (MMSE),[20] and who had objective cognitive impairment not to fulfil the MCI criteria were excluded (n = 1061). In the end, participants who completed all assessments in the present study were eligible for inclusion (n = 3400). The ethics committee of the National Center for Geriatrics and Gerontology approved this study.

MCI criteria

MCI criteria were those established and revised by Petersen,[3] so that participants satisfied the following conditions: (i) subjective cognitive complaints; (ii) objective cognitive decline; (iii) intact general cognitive function; and (iv) functioned independently in ADL. Intact general cognitive function was defined as having a MMSE score >23.[20] Not having dementia was based on not being diagnosed, having intact general cognitive function and functioned independently in ADL (based on the interview about independency in daily activities; eating/feeding, dressing, bathing and showering, functional mobility, up and down of stairs, personal hygiene and grooming, and toilet hygiene). Objective cognitive decline was defined as cognitive function more than 1.5 standard deviations below the reference threshold of any of the tests in the National Center for Geriatrics and Gerontology Functional Assessment Tool.[21] Standardized thresholds for the definition of impairment in the corresponding domain (score <1.5 SD below the age-specific mean) and normal scores were taken from the OSHPE database of healthy individuals,[19] who were independent with basic ADL, did not have medical history of neurological disease (stroke, Parkinson's disease, depression and dementia) and had intact general cognitive function defined as having a MMSE score >23.[20]

Cognitive function

Cognitive function was comprehensively assessed using the National Center for Geriatrics and Gerontology Functional Assessment Tool, and the detailed methodology has been described in a previous study.[21] The test consists of tasks to assess memory, processing speed, attention and executive function, and visuospatial cognition (figure selection). Memory was assessed by using the word and story test. Both tests had two sessions (immediate session and delayed session). Processing speed was assessed using a tablet version of the Symbol Digit Substitution Task (SDST).[21] Attention and executive function were evaluated using a tablet version of the Trail Making Test Part A and B (TMT-B; 15 stimuli).[21] In the Figure selection task, participants were required to select an identical figure from three choices shown at the bottom of the display.[21] Better performance is represented by lower values in the TMT-A & B, and higher values in the other tests.

Gait speed

Walking speed was measured as an indicator of motor function. Participants were asked to walk on a straight walkway 6.6 m in length on a flat floor at their usual walking speed. Walking time was measured over a 2.4-m distance between marks at 2.1 and 4.5 m from the start of the walkway, and the mean walking speed (m/s) was calculated. The cut-off value (1.0 m/s) for slow gait speed was based on this value being discriminative of functional decline in the previous study.[22]

Falling and other covariates

Fall history was collected in a face-to-face interview. A fall was defined as "an unexpected event in which the

person comes to rest on the ground, floor, or lower level".[23] The question "Do you have any history of a fall within the past year?" was used for detecting fallers. For each faller, the number of times was assessed and participants who had more than a twice a year fall history were categorized as "fallers" and others as "not fallers." The definition of faller was defined not to include a single faller, because multiple falls are associated with an intrinsic predisposition to falling, whereas isolated falls are not.[24] Age, sex, body mass index (weight/height^2) and educational history were recorded as demographic data. Medical conditions including current medications and lifestyle were recorded using a questionnaire. The questionnaire also inquired about educational history. Physical activity was assessed as the total amount of time spent walking in a day, using a subscale of the International Physical Activity Questionnaire.[25] In addition, we measured the Geriatric Depression Scale (GDS) score to assess depressive symptoms.[26]

Statistical analysis

We categorized participants into four groups: control subjects without slow gait and MCI (control), subjects with slow gait group and without MCI (SG), subjects with MCI and without slow gait (MCI), and subjects with MCI with slow gait (MCI+SG). We compared participant characteristics between groups using ANOVA for continuous variables and χ^2-tests for categorical variables. Post-hoc analysis of ANOVA was carried out using the Tukey honest significant difference test. To compare cognitive function between groups we used ANOVA, and post-hoc analysis was also carried out. Additionally, to compare cognitive function, we used a general linear model adjusted for participants' characteristics that differed significantly between groups. Multiple logistic regression analysis was carried out to explore independent associations between group characteristic (SG, MCI, MCI+SG) referred to the control group and fallers compared with "not fallers". We calculated odds ratios (OR) and 95% confidence intervals (95% CI) in a crude model as model 1 and in an adjusted model as model 2. Age, sex, body mass index, educational history, medication use, physical activity and GDS score were added sequentially to model 2 as covariates. Analyses in group comparisons were carried out using commercially available software (IBM SPSS statistics software, Version 20; IBM, Chicago, IL, USA). Statistical significance was set at $P < 0.05$ in all analyses.

Results

The 3400 participants (53% women, mean age 71.5 years) were classified as control ($n = 2281$), SG ($n = 278$), MCI ($n = 673$) and MCI+SG ($n = 168$). Table 1 summarizes the demographic data including educational history, medication use, GDS, physical activity, MMSE, WS and fall status. The proportion of women was not significantly different between groups, whereas other characteristics showed significant differences between groups ($P < 0.05$). The MCI+SG group had a higher proportion of recurrent fallers (control 3.3%, SG 7.9%, MCI 5.5%, MCI+SG 9.5%, $P < 0.001$).

The results of post-hoc analysis for each cognitive function are shown in Figure 1. The control group exhibited better performance than the other groups, the SG and MCI groups were not different, and the SG+MCI group showed worse performance than the other groups in SDST ($P < 0.05$). Other cognitive performance domains, including TMT-A and B, figure selection, word memory, and story memory, had similar results in differences between groups, with significantly different performance between each group. These became worse in the following order: control, SG, MCI, SG+MCI ($P < 0.05$). All cognitive functions were significantly associated with the group factor even after adjusting for participants' characteristics ($P < 0.001$).

Logistic analysis showed that the SG, MCI and MCI+SG groups had significant associations with falling, compared with the control group (Table 2). In a crude model, the MCI+SG group had a higher OR (OR 3.05, 95% CI 1.74–5.37) than other groups, although both SG and MCI groups had significant associations with falling as well as the MCI+SG group ($P < 0.05$). The combined effect of SG and MCI was confirmed even in the model adjusted for several covariates (OR 1.99, 95% CI 1.08–3.65).

Discussion

The results of the present study show the association of the combined status of slow gait and MCI with worsened cognitive functioning and with falling. The comparison between groups showed that slow gait had additional effects on cognitive function among subjects with only MCI. Subjects with both MCI and slow gait had worse cognitive functioning than the other groups, even the group with only MCI without slow walking speed. This tendency was not dependent on a specific domain in cognitive function. The combined effect of slow gait and MCI was also found in association with falling, and there was a higher OR between falling and the combination status of slow gait and MCI, compared with either a slow gait or MCI status alone.

Slow gait was associated with poor cognitive function separate from MCI. This result was observed in comprehensive cognitive function assessments, including visuospatial skill, processing speed, attention, executive function and memory. Emerging evidence has shown that slow gait speed is related to cognitive deficits in processing speed, attention and executive function,[7,27]

Table 1 Participant characteristics

Variables	Mean (SD) or %					*P*-value
	Total (n = 3400)	Control (n = 2281)	SG (n = 278)	MCI (n = 673)	MCI + SG (n = 168)	
Age (years)	71.5 (5.2)	70.8 (4.7)	75.5 (6.5)†	71.0 (4.7)‡	75.6 (6.8)†§	<0.001
Sex, (% women)	53.1	53.4	50.9	51.1	59.5	0.207
Body mass index	23.4 (3.1)	23.3 (3.1)	23.7 (3.3)	23.3 (2.9)	23.8 (3.5)	0.063
Medical condition (%)						
Hypertension	45.1	42.5	56.6	47.5	51.8	<0.001
Heart disease	16.5	14.8	21.6	17.7	26.2	<0.001
Respiratory disease	11.2	11.0	13.0	10.9	11.9	0.765
Diabetes mellitus	13.4	12.4	18.3	12.8	22.0	<0.001
Osteoporosis	11.1	10.0	17.6	10.2	18.0	<0.001
Medication use (n)	1.9 (2.0)	1.7 (1.9)	2.6 (2.3)†	2.0 (2.0)†‡	3.0 (2.4)†§	<0.001
Educational years (yrs)	11.6 (2.5)	12.0 (2.4)	11.5 (2.9)†	11.0 (2.4)†‡	10.1 (2.5)†‡§	<0.001
Geriatric depression scale (score)	2.7 (2.5)	2.4 (2.4)	3.4 (2.6)†	3.0 (2.5)†	4.5 (2.8)†‡§	<0.001
Physical activity (min/day)	285.5 (160.0)	294.1 (161.3)	249.7 (159.5)†	278.7 (155.3)	256.2 (149.1)†	<0.001
MMSE (score)	27.2 (1.9)	27.4 (1.8)	27.0 (1.8)†	26.7 (1.8)†‡	26.1 (1.8)†‡§	<0.001
Walking speed (m/s)	1.22 (0.21)	1.28 (0.16)	0.88 (0.10)†	1.27 (0.16)‡	0.86 (0.13)†§	<0.001
Fall (% multiple faller)	4.4	3.3	7.9	5.5	9.5	<0.001

†Significant differences compared with the control group, post-hoc analysis using Tukey test ($P < 0.05$). ‡Significant differences compared with slow gait (SG), post-hoc analysis using Tukey Test ($P < 0.05$). §Significant differences compared with mild cognitive impairment (MCI), post-hoc analysis using Tukey Test ($P < 0.05$). Group differences were tested using ANOVA or χ^2-test. MCI + SG, mild cognitive impairment with slow gait; MMSE, Mini-Mental State Examination; SD, standard deviation.

and to gray matter volume in the prefrontal lobe,[28] which is a crucial region for these cognitive functions. Although there is not full consensus on the association between gait speed and the other domains in cognitive function, particularly memory, Mielke *et al.* suggested that slow gait speed is related to cognitive decline in a comprehensive range of domains including processing speed, attention/executive function, memory and visuospatial recognition.[7] Our current results have expanded the evidence for this, and also have suggested that the effects of slow gait speed might have an impact not in a specific cognitive function, but across a comprehensive range of cognitive functions.

The combination of slow gait and MCI was associated with comprehensive cognitive function decline, even compared with pure MCI without slow gait. To our knowledge, the present study is the first study investigating the combined effects of slow gait and MCI on cognitive performance and falling. The interrelationship between gait and cognition is based on the concepts that gait control itself requires a high order of cognitive processing, and that impaired walking ability represents common pathophysiological deficits, which also affect cognitive function.[18] The present study also supported the notion that decline in motor function combined with cognitive deficits was strongly associated with decreased cognitive function.

Additionally, slow gait and MCI together showed an increased association with falling. Much evidence from epidemiology to an intervention study has shown that deficits of both motor and cognitive function are independently related to fall risk among older adults.[6,13] Although the investigations of falling among MCI subjects are relatively few, and there has been some debate, the present results are in line with other evidence to show that even the status of MCI alone is associated with falling.[14] In a recent systematic review, white matter hyperintensities were associated with physical function and with falling, reflecting pathophysiological changes in the brain.[11] Zheng *et al.* suggested that white matter hyperintensities could independently predict falling incidents as well as cognitive function.[29] Gait speed is a widely accepted measurement to capture functional ability among older adults. Thus, for carrying out a more effective and accurate assessment of risk among MCI subjects, assessment of gait might be useful, and contribute to a better understanding and identification of high-risk individuals.

The present study had some limitations. Because a cross-sectional design was used, the causal relationship between motoric cognitive syndrome and cognitive function should be further investigated, and prospective studies are required to address this issue. Additionally, this study assessed fall history by interview, which could have recall bias. Thus, a study to carry out a daily record of falling prospectively is required. Next, neuroimaging methods have recently been used to clarify cortical control of gait. Pathophysiology of white

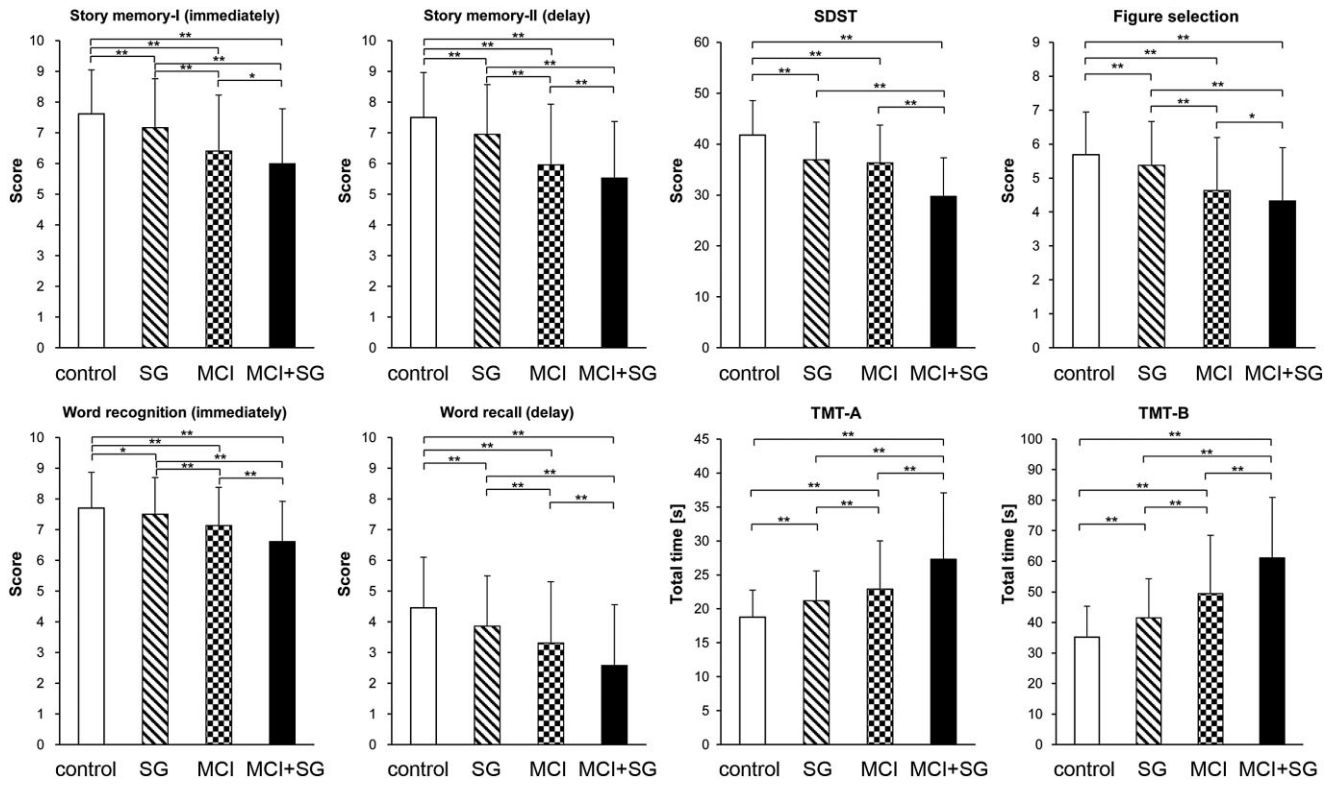

Figure 1 Comparison of cognitive functions assessed by the tablet version of neuropsychological tests between each group. *Compared between groups using the Tukey honest significant difference test, $P < 0.05$. **Compared between groups using the Tukey honest significant difference test, $P < 0.01$. MCI, mild cognitive impairment; MCI+SG, mild cognitive impairment with slow gait; SDST, Symbol Digit Substitution Task; SG, slow gait; TMT-A, Trail Making Test Part A; TMT-B, Trail Making Test Part B.

Table 2 Status of slow gait and mild cognitive impairment associated with fall

Group	Odds ratio (95% confidence interval)	
	Model 1	Model 2
MCI + SG	3.05 (1.74–5.37)**	1.99 (1.08–3.65)*
MCI	1.69 (1.13–2.53)*	1.56 (1.03–2.37)*
SG	2.49 (1.53–4.08)**	1.79 (1.05–3.06)*
Control	Reference	Reference

*$P < 0.05$, **$P < 0.01$. Model 1: Crude model; Model 2: Adjusted for age, sex, educational history, body mass index, medication uses, physical activity, Geriatric Depression Scale. MCI, mild cognitive impairment; MCI + SG, mild cognitive impairment with slow gait; SG, slow gait.

matter lesions or other cognitive disorder; for example, dementia with Lewy bodies, was thought to be associated with falling. Furthermore, MCI subjects had higher risks of having this pathophysiology. Further evidence including imaging techniques should be gathered to clarify the association between cognitive function and gait ability under varied conditions. Then, gait ability could be represented not only by gait speed, but by other gait variables; for example, stride length, stride time and their variability. The effects of deficits in these variables on cognitive function should also be investigated. Finally, the present study also had a common limitation among studies regarding MCI. There were differences between studies in neuropsychological assessments used to define MCI. Subjects' characteristics could be depend on these assessments, and this problem might make it difficult to compare results of studies among MCI. Thus, further evidence would be required.

In conclusion, slow gait speed was associated with cognitive function separately from MCI. The combined status of slow gait speed and MCI was associated with decreased cognitive performance over a comprehensive range of functions and with falling even adjusting for several covariates. Slow gait would be a crucial status variable among MCI subjects. Further studies are required to clarify the interrelationship of gait and cognition.

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