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Aging Clinical and Experimental Research

Does a multicomponent exercise program improve dual-task performance in amnestic mild cognitive impairment? A randomized controlled trial

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ABSTRACT. ***Background and aims:*** *There has been much interest in exercise interventions as a primary behavioral prevention strategy against cognitive decline. The aim of this study was to evaluate the effect of a multicomponent exercise program on physical and dual-task performances in community-dwelling older adults with amnestic mild cognitive impairment (aMCI).* ***Methods:*** *Fifty older adults (23 women) with aMCI (mean age, 76 years) were randomized to an intervention (n=25) or a control group (n=25). The intervention group received a multicomponent exercise program for 90 minutes/day, 2 days/week, or 40 times over six months. The multicomponent exercises included aerobic exercise, muscle strength training and postural balance retraining, which was conducted under multi-task conditions to stimulate attention and memory. Participants in the control group attended two health promotion education classes within six months. Physical and dual-task performances were measured before randomization and after six months. Dual-task performances using reaction times with balance and cognitive demands were measured.* ***Results:*** *The improvement effects on dual-task performances with both balance and cognitive demands were not statistically significant: reaction time with balance demand $F_{1,45}=3.3$, p=0.07, and cognitive demand $F_{1,45}=2.6$, p=0.12. However, there was a significant group-by-time interaction on maximal walking speed, which decreased significantly in the control group ($F_{1,45}=5.9$, p=0.02).* ***Conclusion:*** *This six-month multicomponent exercise program improved maximal walking speed in older adults with aMCI; however, it did not improve dual-task performances assessed by reaction times.*

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INTRODUCTION

Alzheimer's disease (AD) is the most common form of dementia. The presence of mild cognitive impairment (MCI) is associated with an elevated risk of developing AD (1). Along with amnesia, declines in executive function, such as attentional control, are the earliest symptoms of dementia (2). Many studies have used a dual-task paradigm to examine the deficits in attention-related cognitive performance among older MCI and AD patients (3, 4); dual-task performance is recognized as an early marker for dementia (5, 6).

There has been much interest in exercise interventions as a primary behavioral prevention strategy against cognitive decline. This is because recent randomized exercise trials have shown that aerobic-based exercise training enhances physical health and brain health among healthy older adults (7, 8). Exercise interventions, including the enhancement of physical activity, are effective for improving cognitive function in older adults with cognitive impairment (9-11). However, the effects of exercise interventions on physical health are still unclear for older adults with cognitive impairment. In addition, a recent study of geriatric patients with mild to moderate dementia demonstrated that specific dual-task training improved

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Key words: Exercise, dual-task interference, cognitive impairment, reaction time.

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dual-task performance; this study evaluated walking under complex conditions with concurrent cognitive tasks (serial 3 backward calculations) (12). However, dual-task training interventions are too specific as primary behavioral prevention strategies for the general aged population. On the other hand, conventional exercise training – such as resistance, toning, and functional training – is a simply and cost effective method for older adults in clinical community-base settings; regrettably, it has not shown any effect on dual-task performance (13, 14).

We hypothesized that a multicomponent exercise program, consisting of aerobic exercise, muscle strength training and postural balance retraining, might prevent age-related declines in physical and cognitive functioning, including dual-task performance. Although previous evidence showed that multicomponent programs including several type of exercise improved physical functioning in older adults (15, 16), the effect of multicomponent programs, combined exercise, and dual-task training on dual-task performances is still unclear. Previous meta-analytical reviews suggest that combined aerobic exercise and strength training interventions improve cognitive performance (e.g. attention, working memory) to a greater extent than aerobic exercise alone (8, 17). Adding dual-task training to conventional exercises might improve dual-task performance among older adults with a risk of cognitive impairment. However, there is no evidence about the effects of multicomponent exercise on MCI.

We designed a randomized trial to test whether a six month supervised multicomponent exercise program would improve dual-task performances among older adults with MCI. In particular, we focused on MCI subjects with amnestic type, because previous longitudinal studies suggest that patients with amnestic MCI (aMCI) are more likely to progress to AD when compared with patients who have non-memory MCI (18, 19). The aim of this study was to evaluate the effects of a multicomponent exercise program on the physical and dual-task performances of older adults living in the community with aMCI.

METHODS

Study Design

This study was a randomized, controlled trial conducted over six months; measurements were performed at baseline and six months after the intervention. Participants were randomized to an intervention (IG; n=25) or a control group (CG; n=25) after completion of baseline measurements. The study protocol was approved by the ethics committee of the National Center for Geriatrics and Gerontology.

Participants

Participants in this study were recruited from two volunteer databases (n=1543) with elderly individuals (aged 65 years and over); they were selected either by random sampling, or when they attended a medical check-up in Obu, Japan. For inclusion, participants needed to meet the definition of MCI using the Petersen criteria (20). A total of 528 potential participants exhibiting either a Clinical Dementia Rating (CDR) (21) of 0.5, or existing memory difficulties, were enrolled during the first eligibility assessments. Further inclusion criteria for this study required that the participants were 65 years or older, living independently in the community (i.e. no impairment in activities of daily living), fluent in Japanese with sufficient hearing and visual acuity to participate in examinations, had general cognitive functioning (Mini-Mental State Examination [MMSE] (22) scores between 24 and 30), and met the definition for the amnestic type of MCI. Subjects in this study also exhibited objectively determined memory impairment, by satisfying the definition of aMCI, which was assessed using education-adjusted scores from the Wechsler Memory Scale-Revised (WMS-R) Logical Memory II (23, 24). Exclusion criteria included a history of major psychiatric illness (e.g. schizophrenia or bipolar disorder) and other serious neurological or musculoskeletal diagnoses. One-hundred and thirty-five participants underwent the eligibility assessments, which composed the neuropsychological tests, including the MMSE and WMS-R Logical Memory II, physical performance tests and face-to-face interviews. Eventually, 50 participants (mean age 76.0±7.1 years; range 65-92 years; men n=27, 54%) satisfied the inclusion criteria and were allocated to either the intervention or control groups. Researchers and assessors who carried out the performance tests before randomization and after intervention were blinded towards group allocation. All participants provided written informed consent. Sample characteristics at study entry are provided in Table 1; there were no significant differences in these between the exercise and control groups.

Interventions

The six-month-long, multicomponent exercise program involved biweekly 90-min sessions, with combinations of aerobic exercise, muscle strength training and postural balance retraining. In addition, the exercise program had a focus on promoting exercise and life-style behavior changes. Two trained physiotherapists with expertise in geriatric rehabilitation conducted the intervention sessions. Each supervised session began with a 10-min warm-up period and stretching exercises, followed by 20 min of muscle strengthening. Then, over the next 60 min, the participants performed aerobic exercises, postural balance retraining, and combinations of these.

Before and after each session, physiotherapists conducted a health check of each participant. The physiotherapists and a trained instructor implemented a risk management strategy to deal with any accidents during program. For the aerobic exercises, participants underwent stair-stepping and endurance walking. The mean intensi-

Table 1 - *Baseline demographic and characteristics of trial groups (mean±SD).*

Variable	**Exercise group (n=25)**	**Control group (n=25)**	***p*-value**
Age, years	75.3±7.5	76.8±6.8	0.47
Female, number (%)	12 (48.0)	11 (44.0)	0.78
Education, years	11.1±2.4	11.1±2.4	0.67
IADL, score	5.0±0.2	4.9±0.3	0.56
GDS, score	3.0±2.1	2.6±2.0	0.46
Recent history of falls, number (%)	9 (36.0)	6 (24.0)	0.36
MMSE, score	26.8±1.8	26.6±1.6	0.62
Physical performance tests			
Grip strength, kg	25.2±7.3	23.1±8.4	0.36
One-legged standing time, sec	34.0±25.1	29.3±23.6	0.50
Maximal walking speed, m/s	1.6±0.4	1.6±0.3	0.72
Reaction times			
SRT, ms	626.5±51.9	259.3±39.6	0.80
DRT with balance demand, ms	290.2±88.0	268.3±47.5	0.28
DRT with cognitive demand, ms	417.5±153.9	448.6±151.6	0.48
Dual-task costs			
DTC with balance demand, %	11.8±31.4	4.1±14.8	0.28
DTC with cognitive demand, %	56.5±35.2	77.7±73.1	0.20

IADL: instrumental activities of daily living (subscale of the Tokyo Metropolitan Institute of Gerontology Index of Competence); GDS: Geriatric Depression Scale; MMSE: Mini-Mental State Examination; SRT: simple reaction time; DRT: dual-task reaction time; DTC: dual-task cost. Two group *t*-test for continuous variables and chi-square test for categorical variables.

ty of the aerobic exercise was approximately 60% of maximum heart rate. Eleven of the 40 classes conducted during the six month period included 20-30 min of continuous outdoor walking. Postural balance exercises included tandem walking and side walking on balance boards. In addition, participants underwent combined exercises (e.g. circuit training, including stair-stepping, endurance walking, and walking on balance boards) and performed concurrent cognitive tasks during the exercises (e.g. walking while composing a poem); this was based on the dual-task paradigm. For instance, in the performance of concurrent cognitive tasks during exercise, participants were asked to undergo endurance walking while composing a poem, stair-stepping while counting aloud forward by 3 starting from 0, and walking on narrow balance boards while counting aloud backward by 3 starting from 50. The participants were required to carry out daily home-based muscle strengthening exercises and walking, which were self-monitored using a booklet and pedometer, based on the concept of promoting exercise and behavior change. Mean adherence to the exercise program was 86.9% (including the remaining 24 participants); 19 participants (79.2%) in the exercise group attended our intervention program with greater than 80% adherence.

Participants in the control group attended two health promotion education classes during the study period. The classes provided information about general health promotion; this group did not receive specific information regarding exercise, physical activity or cognitive health.

Outcome measures

All measurements and questionnaires were performed before randomization and after six months. Licensed, trained physiotherapists performed all the physical performance tests.

Physical performance tests were conducted to assess muscle strength, walking speed (WS), and balancing ability. We evaluated hand-grip strength in the dominant hand using a mechanical dynamometer. The one-legged standing (OLS) test is a commonly used balance assessment for postural stability.

For the OLS test, we asked participants to look straight ahead at a dot 50 cm in front of them and then stand on their preferred leg with their eyes open and hands down alongside their trunk; OLS balance was measured as the length of time (0 to 60 sec) that participants were able to stand on one leg (the best result from two trials was used in the statistical analysis).

Walking speed (WS) was measured using a 5 m walking test. The maximum WS of each participant was measured over an 11-m straight and level path. The time taken (in sec) to pass the 5 m mark on the path was used as the participant's score. A 3 m approach was allowed before the starting marker, and an additional 3 m of space was provided after the end marker of the 5 m path; this was to ensure a typical walking pace throughout the task. Participants were instructed to walk the 11 m path at their maximal walking pace. The time to complete the 5 m walking test was measured twice; the better of two trials was used for the statistical analysis.

We measured reaction times (RT) under three conditions that included dual-tasks. The RT was measured under three different conditions: 1) quiet standing (simple-task); 2) counting backwards during quiet standing (dual-task with cognitive demands); and 3) stepping while remaining in place (dual-task with balance demands). First, each participant's RT was measured while in a quiet standing position. RT was defined as the interval between the presentation of a visual stimulus and the onset of a pushing response. During the RT measurements, participants were asked to push a handheld button as quickly as possible following the presentation of a red light stimulus composed of seven small lights (each with a diameter of 5 mm). The experimenter ensured that the participants stood safely and quietly, and then issued the verbal command "ready" as the starting signal; the visual starting signal and verbal command preceded each trial. RT responses were measured by a time counter (PTS-010, DKH Inc., Tokyo, Japan) and displayed in milliseconds (ms). After the participants' reaction time responses were measured in the simple-task condition, the other two tasks were randomly done. In the dual-task condition with cognitive demands, participants were asked to count backwards to the number one, starting from 100, 90, 80, 70, 60, 50, 40, 30, and 20 (selected randomly). In the dual-task condition with balance demands, the participants stepped in place at a self-selected speed and rhythm. RTs were measured three times for each participant in each task condition. Participants practiced once before data collection commenced, and the average RT over three trials was used for the statistical analysis. Decreases in RT responses under dual-task conditions (compared with simple RT), defined as the dual-task cost (DTC), were calculated using the following formula (25):

$$(\text{dual-task RT} - \text{simple RT}) / \text{simple RT} \times 100 \qquad (1)$$

Thus, lower DTC represented better performance under dual-task conditions.

Statistical analyses

The data were evaluated by using the statistical package for Social Sciences (SPSS version 19.0) for Windows. Data were expressed as mean values and standard deviations. Results were considered statistically significant if the 2-tailed p-value was <0.05. Baseline values were compared between IG and CG using the unpaired Student's t-test and chi-square test as appropriate. The changes in dependent variables pre- and post-intervention in the IG and CG were analyzed using an analysis of variance (ANOVA) with repeated-measures. The interaction was examined to assess the differential effect between the exercise and control groups, and *post hoc* analysis of within-subject analysis was conducted using Bonferroni correction. We excluded subjects who did not complete post evaluation in the ANOVA with repeated-measures.

The expected number of eligible subjects met with the calculation of the study sample size was based on an alpha of 5% (two-sided) and a power of 80%. To detect an improvement of 20% on the DTC in older individuals with cognitive decline, SD and intervention effect used for sample calculations were based on results of a previous study (12).

RESULTS

As presented in Figure 1, 50 participants (27 men and 13 women) were included and randomized. One partici-

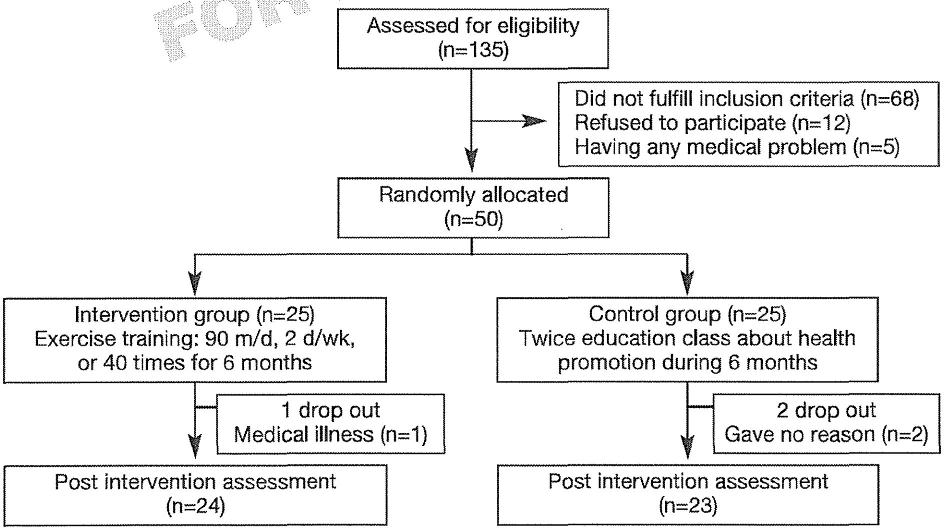

Fig. 1 - *Flow chart of the trial.*

pant in the IC and two participants in the CG dropped out of the post intervention assessment. There were no statistically significant differences in the baseline characteristics, general cognitive function and physical performances (Table 1).

Although there was not a statistically significant main effect for time on maximal walking speed ($F_{1,45}=0.2$, $p=0.64$), group-by-time interaction was statistically significant with decreased significance in the CG ($F_{1,45}=5.9$, $p=0.02$). There was a significant main effect for time on grip strength ($F_{1,45}=5.4$, $p=0.02$), but group-by-time interaction was not significant ($F_{1,45}=0.0$, $p=0.98$). There were no significant improvement effects on one legged-standing time (main effect for time: $F_{1,45}=0.2$, $p=0.69$; group-by-time interaction: $F_{1,45}=0.9$, $p=0.35$). Furthermore, the improvement effects on dual-task performances with both balance and cognitive demands were not statistically significant: reaction time with balance demand (main effect for time: $F_{1,45}=1.2$, $p=0.28$; group-by-time interaction: $F_{1,45}=3.3$, $p=0.07$) and cognitive demand (main effect for time: $F_{1,45}=0.8$, $p=0.37$; group-by-time interaction: $F_{1,45}=2.6$, $p=0.12$), DTC with dual-task balance demand (main effect for time: $F_{1,45}=0.3$, $p=0.62$; group-by-time interaction: $F_{1,45}=2.5$, $p=0.12$) and cognitive demand (main effect for time: $F_{1,45}=0.0$, $p=0.83$; group-by-time interaction: $F_{1,45}=1.5$, $p=0.23$) (Table 2).

DISCUSSION

The results of this study showed no statistically significant effects by our multicomponent exercise program on dual-task performances in older adults with aMCI, although there were significant improvement effects on maximum walking speed.

Previous studies have shown that multicomponent exercise programs are effective interventions for increasing physical performance in the older population. For instance, multidimensional exercise (60 min/day, 2 days/week for 3 months), including resistance band exercises, ball exercises (to increase muscle strength and balance), walking ability training and balance training, showed significant improvements in adductor muscle strength, maximal walking speed, and tandem walking. However, grip strength and the one-legged standing time did not improve among older women with symptoms of geriatric syndrome (15). The collective exercise program using multicomponent physical domains, including walking, strength, balance and flexibility training (60 min/day, 2 days/week for 12 months) has been associated with improvements in mean walking speed, but with no significant effects on the one-legged standing test, nutritional assessment scores and behavioral disturbances in patients with AD (16).

The results of our study, which used a multicomponent exercise program, partially agreed with these other studies. Namely, maximal walking speed improved, but grip strength and one-legged standing time did not improve in the aMCI subjects. A favorable outcome – not reported in previous studies including exercise programs for older adults with MCI or AD (10, 16, 26) – was that we observed better adherence with the study exercise program (mean adherence, 86.9%). However, there were no significant improvement effects on grip strength, one legged-standing time and dual-task performances, although there was a statistically significant group-by-time interaction on maximal walking speed, which decreased significantly in the CG. The intensity of exercise for improving

Table 2 - *Comparison of physical performances, reaction time responses and dual-task costs between the intervention (n=24) and control (n=23) groups after the six month exercise program.*

	Changes from baseline to 6 months		**Analysis of variance for repeated measure**			
Variable	**Exercise group**	**Control group**	**Main effect (time)**	***p*-value**	**Interaction (Group × Time)**	***p*-value**
Physical performances						
Grip strength, kg	1.02±3.18	1.06±3.24	$F_{1,45}=5.4$	0.02	$F_{1,45}=0.0$	0.98
One-legged standing time, s	-2.53±13.75	1.03±11.81	$F_{1,45}=0.2$	0.69	$F_{1,45}=0.9$	0.35
Maximal walking speed, m/s	0.09±0.27	-0.06±0.14[a]	$F_{1,45}=0.2$	0.64	$F_{1,45}=5.9$	0.02
Reaction times						
SRT, ms	-6.92±61.07	-15.74±42.00	$F_{1,45}=2.2$	0.15	$F_{1,45}=0.3$	0.57
DRT with balance demand, ms	-23.82±61.75	6.10±49.39	$F_{1,45}=1.2$	0.28	$F_{1,45}=3.3$	0.07
DRT with cognitive demand, ms	12.15±91.74	-44.30±144.71	$F_{1,45}=0.8$	0.37	$F_{1,45}=2.6$	0.12
Dual-task costs						
DTC with balance demand, %	-4.79±34.79	9.23±24.72	$F_{1,45}=0.3$	0.62	$F_{1,45}=2.5$	0.12
DTC with cognitive demand, %	11.27±38.17	-7.84±66.96	$F_{1,45}=0.0$	0.83	$F_{1,45}=1.5$	0.23

Values are mean±SD. SRT: simple reaction time; DRT: dual-task reaction time; DTC: dual-task cost. [a]Significant differences baseline *vs* after intervention by *post hoc* analysis using Bonferroni correction (within-group differences).

strength and balance ability may have been sub-optimal, because we reserved the majority of time for walking exercise training, within our exercise program. We believe that the lack of intensity and duration of conventional exercise training within the program failed to improve outcomes, besides walking speed.

One of our goals was to evaluate the effect of a multicomponent exercise program on dual-task performance in community-dwelling older adults with aMCI. Our study indicates that our multicomponent exercise program, which included dual-tasking, was ineffective on dual-task performances. Dual-task performances represent and require executive function. A neuroimaging study using functional magnetic resonance imaging examined changes in regional blood flow during dual-task conditions; only the frontal area (especially the dorsolateral prefrontal area) was activated during dual-task conditions (27). In addition, the study used multi-channel functional near-infrared spectroscopy to show that acute moderate exercise increased cognitive performance, and that increasing activation in the dorsolateral prefrontal area coincided with improved cognitive performance (28). Therefore, exercise programs may be effective for increasing brain activations in the prefrontal area, and these processes may potentially improve dual-task performances. A recent non-pharmacologic intervention study using six months of high-intensity aerobic exercise (75% to 85% of heart rate reserve for 45 to 60 minutes/day, 4 days/week for six months) indicated that aerobic exercise improves executive function in aMCI subjects (9). Another intervention study using resistance training (a progressive high-intensity protocol, once-weekly or twice-weekly for 12 months) enhanced the executive function among senior women (26). Our multicomponent exercises were of lower relative intensity, duration and frequency compared to these studies that confirmed the enhancement of exercise interventions on executive function among older people or MCI subjects. This may be one reason why our multicomponent exercises were less effective on dual-task performances. Previous studies have suggested that specific dual-task training improves dual-task performance in older adults with balance impairment (29), fall risk (30, 31) and dementia (12). In contrast, conventional exercise training, such as resistance and functional training, did not affect dual-task performances in earlier studies (13, 14). The intervention effects would appear to be based on task-specific strategies and task-specific training, and on the fact that it is the repetitiveness of a task to be related to the intended outcome (32). For instance, a walking intervention had little effect on the capacity to balance, when performing activities in the clinical balance test that did not require walking (33). Unfortunately, the results of our intervention study using a multicomponent exercise program showed that there were no significant improvement effects on dual-task performances with regard to both balance and cognitive demands. This is in agreement with the results of other studies as well (13, 34). A recent systematic review examined the literature regarding the use of cognitive and cognitive-motor interventions to improve physical functioning in older adults, showing that the lack of effects might be explained by the fact that dual-tasking trainees are not brought to the limits of their performance levels and beyond (35). Lack of specificity because of the dual-task approach used in our multicomponent exercise program may be the cause of the insignificant differences in dual-task performances observed after the intervention. Only 10 to 20% of dual-task training was included in our multicomponent exercise program in this study. We suggest that adding to dual-task training an increased frequency to exercise programs may be the key to improving dual-task performance in older adults with aMCI.

Limitations of this study include no follow-up data after the intervention and small sample size. Also, it should be remembered that the positive effect of knowledge given to the control group during the educational classes might have caused the lack of difference between the groups with respect to outcomes. Lack of consideration for the effects of task prioritization might affect the results of this study. The performance of dual-tasking is affected by task prioritization (36, 37) and depends on several type of capacity, such as the capacity to achieve on primary task, to do well on secondary task, and to do the two tasks together. However, the effects of task prioritization were assessed in this study. Additionally, the results of self-monitoring in a booklet were not reported, but adherence was very high (86.9%). Despite these limitations and the need for further research, the results of this study include important information for intervention strategies using exercise among older adults with aMCI in clinical community-based settings.

CONCLUSIONS

The six-month multicomponent exercise program improved maximal walking speed; however, we found no significant changes in dual-task performances assessed by reaction times in older adults with aMCI after intervention. The task-specific strategies may be effective for improvement of dual-task performances. Further intervention studies are needed to determine how best to improve dual-task performances among older adults with aMCI.

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Gait adaptability and brain activity during unaccustomed treadmill walking in healthy elderly females

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ABSTRACT

This study evaluated brain activity during unaccustomed treadmill walking using positron emission tomography (PET) and [^{18}F]fluorodeoxyglucose. Twenty-four healthy elderly females (75–82 years) participated in this study. Two PET scans were performed after 25 min of rest and after walking for 25 min at 2.0 km/h on a treadmill. Participants were divided into low and high step-length variability groups according to the median coefficient of variation in step length during treadmill walking. We compared the regional changes in brain glucose metabolism between the two groups. The most prominent relative activations during treadmill walking compared to rest in both groups were found in the primary sensorimotor areas, occipital lobe, and anterior and posterior lobe of the cerebellum. The high step-length variability group showed significant relative deactivations in the frontal lobe and the inferior temporal gyrus during treadmill walking. There was a significant relative activation of the primary sensorimotor area in the low step-length variability group compared to the high step-length variability group ($P = 0.022$). Compared to the low step-length variability group, the high step-length variability group exhibited a greater relative deactivation in the white matter of the middle and superior temporal gyrus ($P = 0.032$) and hippocampus ($P = 0.034$) during treadmill walking compared to resting. These results suggest that activation of the primary sensorimotor area, prefrontal area, and temporal lobe, especially the hippocampus, is associated with gait adaptability during unaccustomed treadmill walking.

1. Introduction

Increased gait instability and inconsistency from one step to the next are common in many elderly adults [1,2]. Gait variability, such as the coefficient of variation (CV) in step length [1,2], is a quantifiable feature of walking that is altered in clinical situations, such as falling, frailty, and gait disorders in neurodegenerative diseases [3–5]. The increase in gait instability observed in elderly adults without apparent neurological disease is multifactorial. Age-associated changes may contribute to gait instability, including reduced range of motion, decreased aerobic capacity and muscle function, and impaired balance [6,7]. However, the relationship between gait instability and brain function has not been studied in detail.

Gait is a complex sensorimotor action that is based on automated and reflexive spinal programs that are under the control of several distinct supraspinal centers located in the brainstem, basal ganglia, cerebellum, and cerebral cortex. Several imaging techniques have been developed to identify activation patterns during walking. These include the measurement of glucose metabolism during actual walking using positron emission tomography (PET) with [^{18}F]fluorodeoxyglucose (FDG) [8–10] and single-photon emission tomography (SPECT) with technetium-99m hexamethylpropylene amine oxime or ^{99m}Tc-ethyl cysteinate dimer to measure fixed regional cerebral blood flow [11–13].

Previous PET and SPECT studies revealed that gait disturbance in Parkinson's disease may be associated with underactivity in the medial motor area and cerebellar hemispheres and overactivity in the cerebellar vermis [8,10–12] Recently, it was reported that elderly adults with gait disturbance, secondary to age-related white matter changes, exhibited underactivation

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of the supplementary motor area, thalamus, and basal ganglia compared to elderly adults without gait disturbance [13].

Treadmills are commonly used for gait analysis in clinical and research settings [14]. Treadmill walking, in theory, is mechanically equivalent to overground walking [15,16]. In reality, however, walking on a treadmill can initially be an unfamiliar experience [16,17]. Unimpaired younger adults required 4–6 min to familiarize themselves with the treadmill [14,17]. However, complete familiarization with treadmill in a 15-min single session was not attained in elderly adults [18]. Therefore, a treadmill walking task may be used to investigate the process of adaptation to an unfamiliar environment during walking.

The purpose of the study was, first, to compare the relative brain activation and/or deactivation during treadmill walking compared to resting condition and, second, to determine whether gait adaptability measured as gait variability could be explained through differences of brain activation and/or deactivation in response to an unaccustomed treadmill walk in the elderly adults.

2. Materials and methods

Two hundred and seventy-four females were selected from our database of elderly volunteers ($n = 1289$). Inclusion criteria were: age ≥ 75 years, no history of neurological or psychiatric disorders, cardiovascular disease, hypertension, heart failure, diabetes mellitus, head trauma, drug or alcohol abuse, or severe pain. Of the initial 274 females, 106 completed cognitive and physical performance tests including preferred walking speed. Sixty-nine females were excluded because of low cognitive function (Mini Mental State Examination score < 27 points), multiple medications, drug allergy, and gait disturbance (gait freezing, wide-based gait, or remarkable body sway during gait). Magnetic resonance imaging (MRI) with T1-weighted contrast was performed in 37 females using a 1.5-T Sigma Horizon scanner (GE, Milwaukee, WI, USA). Thirteen females were excluded based on MRI exclusion criteria (cerebrovascular lesions or high cortical atrophy). The remaining 24 females participated in the study (mean age, 78.0 ± 2.3 years; range, 75–82 years).

Participants were fully informed of the purpose and potential risks of the experiments, including radiation dose, and provided written, informed consent. The Ethics Committee of the Tokyo Metropolitan Institute of Gerontology approved the study protocol.

Brain glucose uptake in the rest and treadmill walking conditions was assessed on separate days (within two weeks, at least two days apart). Each condition consisted of three phases: preparation, rest or treadmill walking, and a PET scan. Total time of the FDG–PET measurement was about 85 min in each condition. The preparation period was 40 min in duration, after which the participants either rested for 35 min or walked for 25 min on a treadmill. A 6 min FDG–PET scan was performed subsequently.

During the preparation period, a catheter for injection of FDG was inserted into a vein of the left forearm. FDG (180 MBq) was injected intravenously at the onset of rest and treadmill walking. For the resting condition, participants lay supine with their eyes closed for 35 min. For the treadmill walking condition, participants walked on a treadmill (PW-21; Hitachi, Tokyo, Japan) for 25 min at 2.0 km/h while holding the handrails, to avoid falling during walking and to provide a uniform visual environment. The participants then rested on a bed with their eyes closed for 10 min.

A step counter with an infrared ray device (m-Stride ST-1100; S & ME, Tokyo, Japan) recorded walking speed, cadence, and step length during the treadmill walking period to evaluate temporal changes in gait characteristics. The step counter was placed on side-rail of a treadmill to measure belt speed (cm/s) of the treadmill and step time (s) during treadmill walking using infrared ray. The step length (cm) and cadence (steps/min) were calculated as follows.

$$\text{Step length} = \text{Belt speed} \times \text{Step time}, \tag{1}$$

$$\text{Cadence} = 60/\text{Step time}, \tag{2}$$

Step length was measured for 1 min at 0, 5, 10, 15, 20, and the 24th–25th min. We used 200 steps for the analysis of step length and cadence, 50 steps from each 1 min period starting at the 10th–11th min, 15th–16th min, 20th–21st min, 24th–25th min of treadmill walking. Five minutes following the rest or walking periods, PET scans were performed using a Headtome-V (SET 2400W, Shimadzu, Kyoto, Japan) in the three-dimensional (3D) mode. This 6 min emission scan therefore occurred 40 min after the intravenous injection of FDG. The scan produced images that had the following parameters: matrix size, $96 \times 96 \times 50$; and voxel size, $2\text{ mm} \times 2\text{ mm} \times 3.125\text{ mm}$. The attenuation was corrected via a transmission scan using a $^{68}\text{Ga}/^{68}\text{Ge}$ source.

The images were reconstructed using a filtered back projection algorithm with a second-order low-pass filter with a cutoff frequency of 1.25 cycles/cm. Corrections were applied for dead time and detector non-uniformity. Image processing and data analysis were performed using statistical parametric mapping (SPM8 software, Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London, UK) implemented on MATLAB (MathWorks, Natick, MA, USA). The tasks performed using SPM8 were MRI/PET coregistration, spatial normalization, spatial smoothing, MRI segmentation, normalization, and SPM analysis. Anatomical brain MR images were spatially normalized into the Montreal Neurological Institute (MNI, McGill University, Montreal, Canada) standard template using an affine transformation (12 parameters for rigid transformations) [19]. The parameters were applied to the coregistered FDG–PET images. Therefore, all stereotactic coordinates given in this paper refer to the MNI coordinate system. Subsequently, the spatially normalized images were blurred with a Gaussian filter (FWHM 12 mm) to increase signal-to-noise ratio. All scans were analyzed after normalization to the white matter. The normalization prior to voxel-based statistics was performed using an anatomical mask in MNI space. This normalization was used for all participants to remove the effects of differences in the overall counts. The pixel values were normalized by scaling the activity in each pixel in proportion to the global activity. This ensured that the variance related to the substantially different global activity between high- and low-dose images was stabilized. In this process, the mean global activity of each scan was adjusted to 50. Planned comparisons between the rest and exercise conditions were performed using t statistics for each voxel. These analyses generated statistical parametric maps of the t statistic (SPM $\{t\}$), which were subsequently converted to unit normal distribution (SPM $\{Z\}$). The estimated final spatial resolution was $19\text{ mm} \times 21\text{ mm} \times 18\text{ mm}$.

The standard deviation for the CV, the ratio of the standard deviation to the mean, in step length during the treadmill walk was large in our sample (mean $7.2 \pm 6.0\%$). However, there was a bimodal distribution around the median value for the CV for step length and it was therefore appropriate to use the median step length for CV as the cut-point dividing the females into low step-length variability (LSV) and high step-length variability (HSV) groups. Student's t test was used to compare age and gait variables between the LSV and HSV groups during treadmill walking. The significance threshold was set at $P < 0.05$. SPSS version 19 (Chicago, IL, USA) was used for statistical analyses.

The locations of relatively activated and deactivated brain areas were identified and listed according to stereotaxic coordinates and visual inspection of the structural MRI provided by SPM8. Significant relative increase (walk > rest) and decrease (rest > walk) in cerebral glucose uptake during the gait condition compared with the rest condition were explored for each group separately. Both relative increases and decreases in glucose metabolism were calculated and considered significant at $P < 0.05$, and were corrected for multiple comparisons using a familywise error (FWE) method [20].

A region of interest (ROI) analysis was used to assess activated and deactivated brain areas during treadmill walking between the HSV and LSV groups, which were interpreted as the relative difference in gait-induced glucose uptake changes between groups. The ROIs were determined on visually apparent regions of relative activation (walk > rest) and deactivation (rest > walk) images for all participants. Glucose metabolism in the ROIs was measured based on the standardized uptake value (SUV), which was defined as follows.

$$\text{SUV} = C/D/w, \tag{3}$$

where C represents the radioactive concentration in the tissue (Bq/mL), D represents the injected dose (Bq), and w represents body mass (g) [21]. FDG dose was adjusted to body weight. Student's t test was used to compare the SUV between the LSV and HSV groups. The significance threshold was set at $P < 0.05$ during between-group comparisons in specific regions. The ROI analysis was performed using the Dr. View software (AJS, Tokyo, Japan). The anatomical designations used to the Talairach Client and MRI atlas of human white matter [22].

3. Results

There was no difference in age between the LSV and the HSV groups (77.4 ± 2.3 versus 78.7 ± 2.2 years; $P = 0.19$) or the following treadmill variables: walking speed (34.7 ± 0.4 versus 34.4 ± 0.5 m/min; $P = 0.26$), cadence (101.4 ± 15.1 versus 96.0 ± 15.7 steps/min; $P = 0.39$), and step length (34.9 ± 5.2 versus 37.4 ± 6.4 cm; $P = 0.31$). The HSV group had a higher step length CV compared to the LSV group (2.7 ± 0.8 versus 11.8 ± 5.5; $P < 0.001$).

The most prominent relative activations during treadmill walking in the LSV group were found in the primary sensorimotor areas (Broadman area (BA) 3 and 4), occipital lobe (BA 17, 18, and 19), and anterior and posterior lobe of the cerebellum compared with the resting condition (Table 1, Fig. 1A). The LSV group did not

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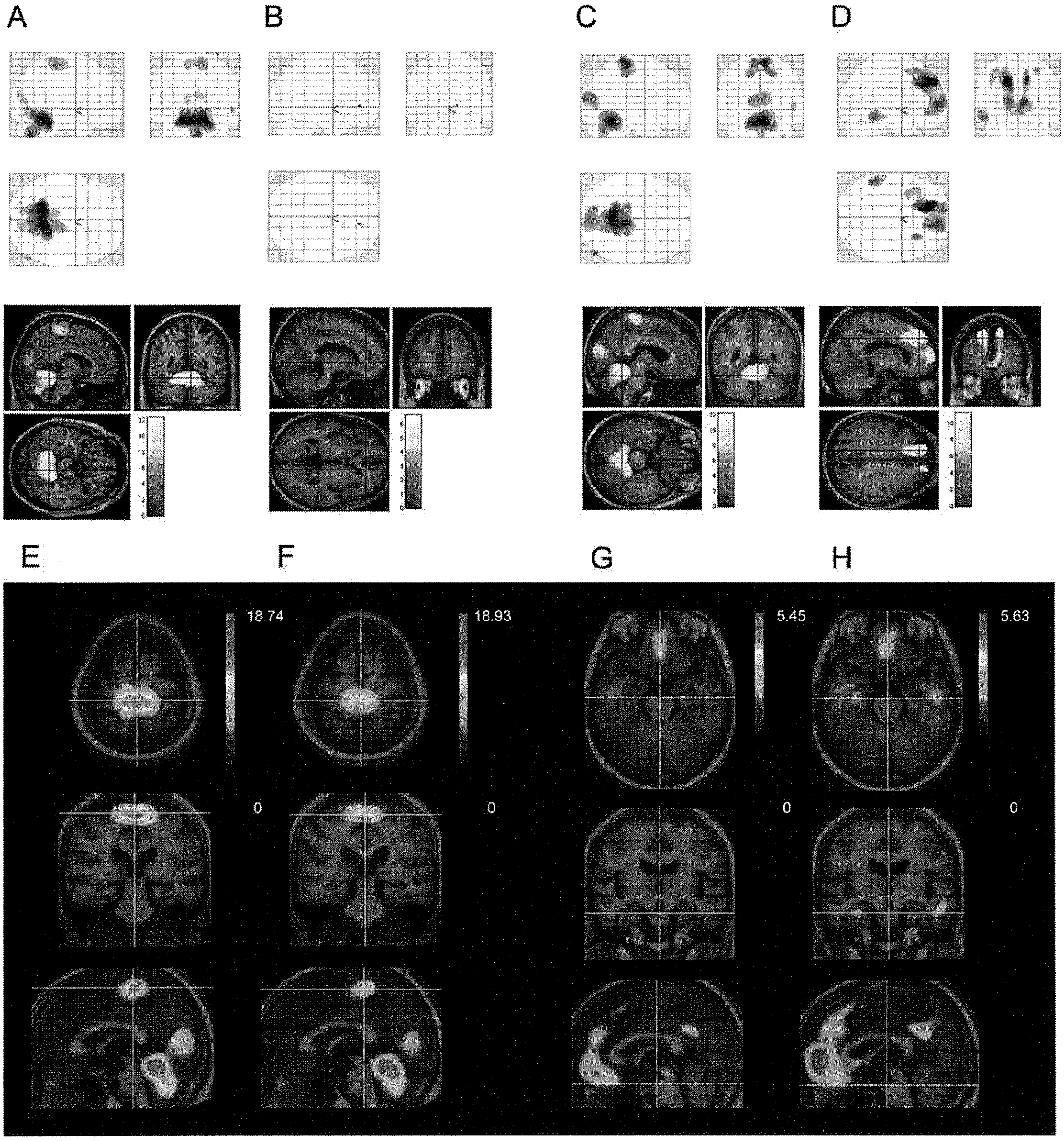

Fig. 1. FDG–PET activations and deactivations during treadmill walking in the LSV and HSV groups. During treadmill walking in the LSV group, activations (A) were prominent in the primary motor areas, visual cortical areas and anterior and posterior lobe of cerebellar. Slight deactivation (B) was found in the right sub-gyral. In the HSV group, activations (C) were prominent in the primary motor areas, visual cortical areas and anterior and posterior lobe of cerebellar. Deactivations (D) were found in the supplementary motor areas (superior and medial frontal cortex, dorsolateral prefrontal cortex). The primary sensorimotor cortex was activated more during treadmill walking versus the resting condition, in the LSV group (E) compared to the HSV group (F). Hippocampus and temporal lobe were deactivated more for treadmill walking versus the resting condition, in the HSV (H) group compared to the LSV group (G).

exhibit prominent relative deactivation during treadmill walking compared with the resting condition (Table 1, Fig. 1B)

The HSV group exhibited marked relative activation in the primary sensorimotor areas (BA 3 and 4), occipital lobe (BA 17, 18, and 19), and anterior and posterior lobe of the cerebellum during treadmill walking compared with the resting condition (Table 2, Fig. 1C). However, the HSV group showed relative deactivation in some regions during treadmill walking. The most prominent relative deactivations during treadmill walking were found in the frontal lobe, including the dorsolateral prefrontal cortex (BA 9 and 46), supplementary motor area (BA 6 and 8), and inferior temporal gyrus (Table 2, Fig. 1D).

Lower panels of Fig. 1 show FDG images of relative activations and deactivations during treadmill walking compared with the resting condition in the participants of the LSV and HSV groups. The SUV uptakes of the relatively activated and deactivated regions are shown in Table 3. The primary sensorimotor areas (BA 3 and 4), occipital lobe (BA 17, 18, and 19), and cerebellum (especially the vermis) were activated during treadmill walking. Relative deactivation of FDG was observed in the orbitofrontal cortex (BA 11), superior frontal gyrus (BA 10), dorsolateral prefrontal cortex (BA 9 and 46), supplementary motor area (BA 6 and 8), middle and superior temporal gyrus white matter, posterior cingulate cortex (BA 31), pons, and hippocampus in all participants. A detailed comparison of the relative activations and deactivations using ROI analysis revealed a more prominent activation of the primary sensorimotor area in the LSV group (Table 3, Fig. 1E) compared with the HSV group (Table 3, Fig. 1F) ($P = 0.02$). The HSV group

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Table 1
FDG activations and deactivations during treadmill walking in the low step-length variability group.

(a) FDG activation during treadmill walking in the low step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	*Z*	*T*	*p*	*x*	*y*	*z*
Left cerebellum, anterior lobe, culmen		5196	6.57	12.26	<0.001	−20	−52	−16
Right cerebellum, anterior lobe, culmen			6.46	11.75	<0.001	12	−46	−16
Right cerebellum, posterior lobe, inferior semi-lunar lobule			5.83	9.4	<0.001	4	−68	−38
Right cerebrum, frontal lobe, precentral gyrus		936	5.44	8.22	0.001	10	−30	66
Left cerebrum, parietal lobe, postcentral gyrus	3		4.84	6.69	0.014	−10	−32	66
Right cerebrum, occipital lobe, inferior occipital gyrus	19	39	5.17	7.48	0.004	56	−72	−2
Right cerebellum, posterior lobe		57	4.89	6.8	0.011	20	−50	−58
Left cerebrum, occipital lobe, superior occipital gyrus, cuneus	17	130	4.82	6.63	0.015	−14	−78	12
Right cerebrum, occipital lobe, cuneus	18	147	4.68	6.31	0.027	8	−84	16
Left cerebellum, posterior lobe		4	4.64	6.24	0.03	−24	−84	−46
Left cerebellum, posterior lobe		23	4.63	6.21	0.032	−20	−52	−56
Right cerebrum, occipital lobe, middle or lateral occipital gyrus	19	1	4.54	6.02	0.045	28	−86	38

(b) FDG deactivation during treadmill walking in the low step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	*Z*	*T*	*p*	*x*	*y*	*z*
Right cerebrum, frontal lobe, genu of the corpus callosum		5	4.82	6.64	0.015	12	40	0

(Table 3, Fig. 1H) showed relative deactivation in the middle and superior temporal gyrus white matter ($P = 0.03$) and hippocampus ($P = 0.03$) during treadmill walking compared with resting than did the LSV group (Table 3, Fig. 1G). There were no significant differences in occipital lobe, cerebellum, frontal lobe, posterior cingulate cortex, and pons between groups.

4. Discussion

This study examined changes in whole brain glucose metabolism using FDG-PET during rest and unaccustomed treadmill walking in healthy elderly females, classified as either low or high step-length variability walkers. The main findings of the study were that females with high step-length variability showed relative deactivations in the supplementary motor areas and dorsolateral prefrontal cortex compared to rest and that females with low step-length variability exhibited greater relative activations in the primary motor area during treadmill walking compared to the HSV group. The HSV group showed greater relative deactivations in the temporal lobe, especially in the hippocampus, during treadmill walking compared with the LSV group.

Hanakawa [23] proposed a hypothesis regarding the neural mechanisms that control human bipedal gait. This author postulated that multiple channels from the basal ganglia–thalamocortical system and basal ganglia–brainstem system are involved in the regulation of the central pattern generator (CPG) in the spinal cord (Fig. 2). In the present study, the most prominent relative activations during treadmill walking were found in the primary sensorimotor areas, occipital lobe, and cerebellar areas for both groups. The primary motor area projects to the spinal cord through the corticospinal tract, and it is believed that the primary motor area is involved in the precise control of limb movement during walking. The coordination of limb and trunk movements to adjust for a shift in the center of gravity associated with locomotion may be one of the primary functions of the cerebellum in gait control. Previous neuroimaging experiments have shown that the cerebellar vermis and the anteromedial part of the cerebellar hemispheres are bilaterally activated during walking in healthy individuals [9,11,12]. The cerebellum is able to make immediate alterations in ongoing movement patterns [24]. It functions as a real-time sensory processing device and modulates motor responses in a reactive or feedback manner based on sensory perturbations [25].

Our findings also suggest that the cerebellum plays an important role in gait adaptation to unfamiliar environments, such as walking on a treadmill. The occipital lobe, including the

Table 2
FDG activations and deactivations during treadmill walking in the high step-length variability group.

(a) FDG activation during treadmill walking in the high step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	*Z*	*T*	*p*	*x*	*y*	*z*
Right cerebellum, anterior lobe, culmen		3715	6.54	12.12	<0.001	0	−50	−18
Right cerebrum, parietal lobe, postcentral gyrus	6	1878	6.37	11.38	<0.001	8	−32	72
Left cerebrum, parietal lobe, postcentral gyrus	3		5.75	9.16	<0.001	−10	−34	72
Left cerebrum, parietal lobe, postcentral gyrus white matter			5.4	8.09	0.001	−14	−28	54
Right cerebrum, occipital lobe, cuneus		1402	5.52	8.46	0.001	2	−84	18
Left cerebrum, occipital lobe, cuneus			5.47	8.29	0.001	−6	−82	14
Right cerebrum, occipital lobe, middle or lateral occipital gyrus		60	5.06	7.2	0.005	52	−78	4
Left cerebellum, posterior lobe		40	4.74	6.45	0.017	−22	−46	−52
Right cerebellum, posterior lobe		7	4.67	6.3	0.022	36	−84	−40
Right cerebrum, occipital lobe, middle or lateral occipital gyrus	17	3	4.52	5.99	0.039	26	−100	−12

(b) FDG deactivation during treadmill walking in the high step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	*Z*	*T*	*p*	*x*	*y*	*z*
Left cerebrum, frontal lobe, superior frontal gyrus		5131	6.31	11.14	<0.001	−18	46	40
Right cerebrum, frontal lobe, superior frontal gyrus white matter			5.74	9.13	<0.001	10	60	6
Right cerebrum, frontal lobe, superior frontal gyrus	8		5.7	8.98	<0.001	12	54	40
Left cerebrum, temporal lobe, inferior temporal gyrus		397	5.62	8.74	<0.001	−52	−44	−14
Right cerebrum, frontal lobe, middle frontal gyrus	6	113	5.38	8.04	0.001	30	22	58

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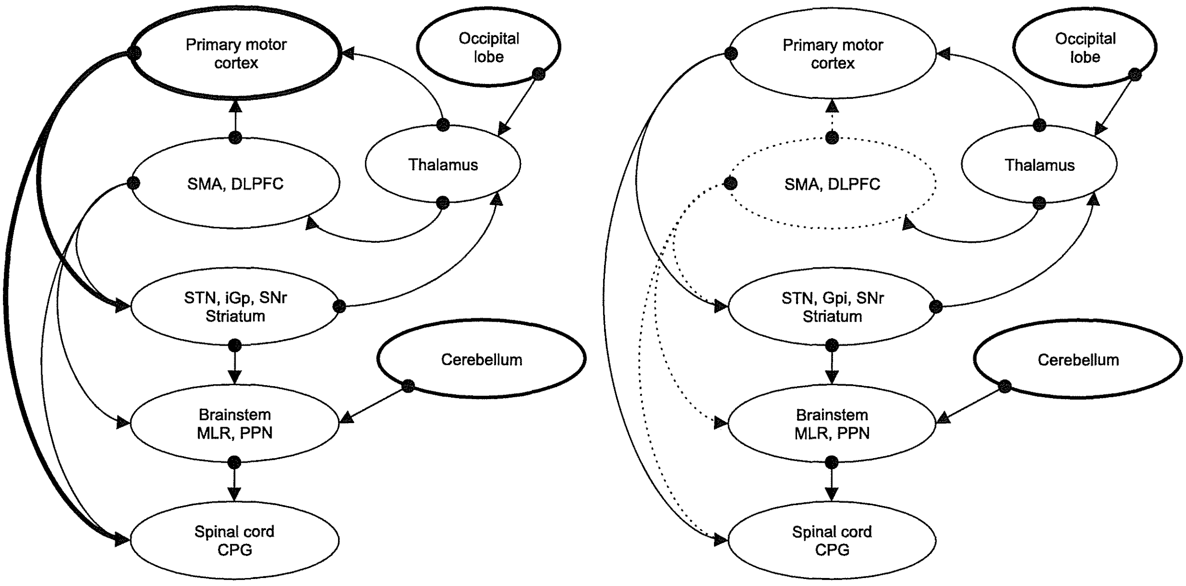

Fig. 2. Differences in neural mechanisms controlling treadmill walking in LSV compared to HSV individuals. Multiple channels from the 'basal ganglia–thalamo-cortical system' and 'basal ganglia–brainstem system' are both involved in regulating the central pattern generator (CPG) in the spinal cord. The primary motor cortex and non-primary motor areas such as supplementary motor areas constitute multiple parallel circuits with the basal ganglia counterparts. (a) Left panel displays our hypothesized neural network for the LSV group. The projections from M1 increased during walking to adapt to the unaccustomed environment (treadmill walking). (b) Right panel displays our hypothesized neural network for the HSV group. The HSV group deactivated FDG uptakes in SMA during treadmill walking and the deactivations may lead to dysfunction of 'basal ganglia–thalamo-cortical system' and 'basal ganglia–brainstem system'. *Abbreviations*: STN, subthalamic nucleus; iGP, internal segment of globus pallidus; SNr, substantia nigra pars reticulata; MLR, midbrain locomotor region; PPN, pedunculopontine nucleus.

cuneus (BA 17) and precuneus (BA 7/31), is believed to play a role in visuomotor coordination. The areas which showed relative activation were compatible with those reported in a previous activation study using FDG–PET [10]. In addition, online visual feedback was the requisite for locomotor adaptation [26] and was thought to override internal model predictions of control during locomotion [27]. Our study further supports the hypothesis that locomotor adaptation requires neuronal activation in the region related to visuomotor coordination.

In the HSV group, relative deactivations in FDG uptake were observed over a broad area of the prefrontal cortex, including the supplementary motor area and the dorsolateral prefrontal cortex. Cortical locomotor commands originating from the premotor and supplementary motor cortices are conveyed to the brainstem locomotor centers via the basal ganglia. The structure of the dorsolateral prefrontal cortex is important for selecting and planning voluntary movements [28] or simulating motor actions [29]. The relative deactivation of the supplementary motor area and dorsolateral prefrontal cortex may be associated with the finding that the participants in the HSV group might have found it difficult to adapt to an unfamiliar environment, i.e., treadmill walking.

Detailed group comparison revealed that the LSV group had a more prominent relative activation in the primary sensorimotor area compared to the HSV group and that the HSV group exhibited relative deactivation in the hippocampus compared to the LSV group during treadmill walking. The relative activation of the primary motor area may improve projection to the basal ganglia and to the CPG in the spinal cord, thus facilitating the strengthening of the basal ganglia–thalamocortical system during walking (Fig. 2). Regarding relative deactivation in the hippocampus, Zimmerman et al. (2009) found that increased variability in step length was associated with poorer hippocampal metabolism in elderly individuals. The authors suggested

Table 3
A region of interest analysis based on the standardized uptake value as the relative difference in gait-induced glucose uptake changes between groups.

	LSV group Mean (SD)	HSV group Mean (SD)	*p* value
Walk>Rest			
Primary sensorimotor area (BA 3, 4)	13.56 (3.01)	10.93 (2.16)	0.02
Occipital lobe (BA 17, 18, 19)	11.42 (4.29)	9.25 (3.55)	0.19
Cerebellum (vermis, anterior and posterior lobe)	17.18 (4.85)	17.36 (4.07)	0.92
Rest>Walk			
Orbitofrontal cortex (BA 11)	3.85 (3.18)	3.67 (2.94)	0.89
Superior frontal gyrus (BA 10)	4.16 (2.54)	4.76 (2.83)	0.59
Dorsolateral prefrontal cortex (BA 9, 46)	3.16 (2.09)	4.45 (2.25)	0.16
Supplementary motor area (BA 6, 8)	3.79 (1.74)	4.12 (1.83)	0.65
Middle and superior temporal gyrus white matter	1.85 (1.45)	3.07 (1.15)	0.03
Posterior cingulate cortex (BA 31)	3.01 (2.16)	3.67 (3.58)	0.59
Pons	2.40 (1.89)	1.84 (0.94)	0.37
Hippocampus	1.24 (1.31)	2.44 (1.29)	0.03

LSV: high step-length variability; HSV: low step-length variability.

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that the hippocampus plays an important role in the timing or rhythmicity of locomotion, which may be compromised in elderly adults [30]. Additionally, PET study showed that imagined walking with obstacles was associated with increased prefrontal and parahippocampal activation, suggesting that higher brain centers become progressively engaged when the locomotor task demands increased cognitive and sensory information processing [31]. Beauchet et al. (2003) reported that stride-to-stride variability increased significantly in older subjects with the interfering task of counting, although there was no significant change in young subjects. The authors suggested the involvement of higher cortical regions for the motor control of gait under a dual-task in older adults [32]. Our findings therefore support and extend previous research via the identification of an association between FDG–PET activation/deactivation and gait *variability* in an unfamiliar environment in elderly adults. Walking task used a treadmill, as a stimulator to increase cognitive demand may be beneficial tool for identifying the involvement of cortical regulation in gait of the older adults.

Limitations of our study were that the sample was drawn from a larger study of community-dwelling adults over the age of 75 years, and we were not able to examine the relationships between brain activity and cognitive functions across the entire adult lifespan.

In conclusion, FDG PET revealed that the most prominent relative activations during treadmill walking were the primary sensorimotor areas, occipital lobe, and cerebellar areas. The high step-length variability group exhibited a lesser relative activation in the primary sensorimotor area and a greater relative deactivation in the white matter of the middle and superior temporal gyrus and hippocampus during treadmill walking than the low step-length variability group. These results suggested the involvement of cortical regulation in gait adaptation of the older adults. Additional studies are necessary to examine the longitudinal sequence and relationships of gait, cognitive status, and presynaptic functional changes that emerge across the spectrum from normal aging to advanced functional decline.

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Conflict of interest statement

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Performance-based assessments and demand for personal care in older Japanese people: a cross-sectional study

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ABSTRACT

Objectives: To identify appropriate clinical tests for determining the demand for personal care in older Japanese people.

Design: Cross-sectional observation study.

Setting: Obu Study of Health Promotion for the Elderly (Obu, Aichi) and Tsukui Ordered Useful Care for Health (241 day-care centres) cohorts in Japan.

Participants: A total of 10 351 individuals aged 65 years or older (6791 with personal care and 3560 without personal care) participated in the study.

Measures: Physical performance tests included grip strength, the chair stand test, walking speed at a comfortable pace, and the timed up-and-go test. Personal care was defined as participants who had been certified in the national social long-term care insurance in Japan.

Results: Individuals who received personal care showed a significantly poorer performance than those without personal care for all physical performance tests ($p<0.001$). Gait speed was the most useful of the physical performance tests to determine the demand for personal care (receiver operating characteristic curve statistics: men, 0.92; women, 0.94; sensitivity: men, 86; women, 90; specificity: men, 85; women, 85). After adjustment for age, sex, cognitive impairment and other physical tests, all physical performance tests were individually associated with the demand for personal care. A slow gait speed (<1 m/s) was more strongly correlated with the demand for personal care than other performance measures (gait speed OR: 5.9; 95% CI: 5.0 to 6.9).

Conclusions: Clinical tests of physical performance are associated with the demand for personal care in older people. Preventive strategies to maintain physical independence may be required in older adults who show a gait speed slower than 1 m/s. Further research is necessary to confirm these preliminary results.

ARTICLE SUMMARY

Article focus

- Measures of physical performance may identify older persons with a preclinical stage of disability.
- However, it is unclear which performance test and cut-point are the most useful to screen for risk of functional dependence in older Japanese people.
- The purpose of this study was to identify appropriate clinical tests for determining the risk of functional dependence in older Japanese people.

Key messages

- Clinical tests of physical performance were associated with a functional decline in older people.
- Preventive strategies to avoid personal care may be required in older adults who show a gait speed slower than 1 m/s.

Strengths and limitations of this study

- Strengths of this study include a large sample size and performance-based assessment, which could determine actual physical capacity and predict subsequent physical disability in older people living in the community.
- We analysed cross-sectional data. Therefore, further investigation of the validity of these tests in predicting the risk of disability in older people using a prospective study design is recommended.

INTRODUCTION

Japan is the fastest ageing society on earth and the first large country in the history to have its population start shrinking rapidly from natural causes. The life expectancy of Japanese people (mean age: men, 79.4 years; women, 85.9 years) is at the highest level in the world. The population of Japan, which currently stands at 127 million, is expected to fall to just under 100 million in the next 40 years. By 2050, 4 of 10 adults in Japan will be older than 65 years of age. Japan implemented the national social long-term care insurance (LTCI) system on 1 April 2000. Every Japanese person aged 65 and older is eligible for benefits based strictly on physical and mental frailty or disability.[1] In June 2006, the Japanese government implemented a major LTCI reform that focused on preventive benefits for the population at high risk of disability (ie, physical and/or cognitive frailty), to contain the skyrocketing costs of the LTCI.[2]

Physical frailty increases with advancing age and is a major risk factor for dependency, institutionalisation, and mortality.[3–5] People with a disability have higher healthcare needs and use compared with those without a disability.[6] Although the biggest risk factor for future frailty is advancing age, other factors that are possibly modifiable through interventions should not be ignored. For the purpose of targeting risk factors for future frailty, adequate assessment of individual people may be required. One of the main characteristics of the elderly population is its heterogeneity, with elderly people in the same age range showing a wide variance with regard to their risk of disability. To prevent frailty or disability, population-based intervention programmes should be targeted at the population at risk. A feasible and valid screening tool available for research and clinical settings is required to identify target populations. The Interventions on the Frailty Working Group developed recommendations to screen, recruit, evaluate and retain frail older persons in clinical trials.[7] They reported that most researchers focus on the following domains for identification of physical frailty: mobility, such as lower extremity performance and gait abnormalities; muscle weakness; poor exercise tolerance; unstable balance and factors related to body composition, such as weight loss, malnutrition and muscle loss.[7]

In an effort to select tailored preventive programmes in the Japanese LTCI system, those at high risk for subsequent disability are identified by a basic functional status questionnaire. Although the questionnaire is relatively quick to administer, a performance-based assessment could determine actual physical capacity and more accurately predict subsequent physical disability in community-living older people. Guralnik *et al*[8] reported that measures of physical performance may identify older persons with a preclinical stage of disability who may benefit from interventions to prevent the development of frank disability. A previous study identified that a rapid gait test was more likely than other mobility performance tests to discriminate older women at high risk of frailty based on the Japanese LTCI system.[9] However, which performance tests including upper and lower limb muscle functions and which cut-points are the most useful to screen for the demand for personal care are not clear. This study investigated the relationships between performance-based physical assessments and demand for personal care in older people using two large sample cohorts in Japan.

METHODS

Participants

We performed a national study of 10 351 individuals aged 65 years and older who had received personal care (n=6791) and those who had not received personal care (n=3560). The study included individuals who were enrolled in the Obu Study of Health Promotion for the Elderly (OSHPE) and the Tsukui Ordered Useful Care for Health (TOUCH) programme. To enrol in the OSHPE, an individual was recruited from Obu, Japan, which is a residential suburb of Nagoya. Inclusion criteria required that the participant was aged 65 years or older at examination in 2011 or 2012, lived in Obu, and had not participated in another study. Exclusion criteria stipulated that participants be certified as needing support or care by the Japanese public LTCI system, had disability in basic activities of daily living, and could not carry out performance-based assessments. To enrol in the TOUCH programme, an individual had to be 65 years or older and certified as needing support or care from the Japanese public LTCI system. Detailed information was provided in a previous study.[10] In brief, TOUCH sites (241 day-care centres) are located throughout Japan and provide comprehensive, facility-based day-care services (eg, bath, lunch, physical and cognitive recreational activities and physical exercise). Most TOUCH clients have some physical disability and frailty, defined as the presence of weakness, low physical activity and/or slow gait speed, in accordance with the widely accepted definition of frailty.[7]

A total of 10 351 older participants (mean age, 78.8±8.0 years) underwent performance-based assessments. Informed consent was obtained from all participants prior to their inclusion in the study, and the Ethics Committee of the National Centre for Geriatrics and Gerontology approved the study protocol.

Performance-based assessment

The assessment measures were conducted by well-trained staff who had nursing, physiotherapy, occupational therapy or similar qualifications. Prior to start of the study, all staff received training from the authors in the correct protocols for administering all of the assessment measures. The assessment included several physical tests. Upper and lower limb muscle functions were assessed with the grip strength (GS) and the chair stand test (CST), respectively.[11] Gait function was assessed with walking time tests conducted at a comfortable pace (comfortable walking speed, CWS) and with the timed up-and-go (TUG) test.[12]

GS was measured in kilograms in the participant's dominant hand using a Smedley-type handheld dynamometer (GRIP-D; Takei Ltd, Niigata, Japan). The CST involved sitting down and standing up five times, using a chair without an armrest. The score was the time taken to complete the task in seconds. Participants were asked to exert their maximum effort in GS and CST. CWS was measured in seconds with a stopwatch. Participants were asked to walk on a flat and straight surface at their CWS. Two markers were used to indicate the start and end of the path, and a 2 m and over approach was allowed before reaching the start marker so that participants can walk at their comfortable pace within the timed path. They were instructed to continue walking past the end of the path for a further 2 m and over to ensure that the walking pace was consistent throughout the task. The TUG test involved rising from a chair, walking 3 m, turning around, walking back to the chair and sitting down.[12] The TUG test is one of the most frequently used tests of balance and gait, and is often used to assess fall risk in older people.[13] The time to complete the TUG test was measured, in seconds, at each participant's usual pace. Both walking tests were measured once, and if a walking aid was nomally used inside the home, this aid was used during the tests.

Cognitive function

The Mini-Mental State Examination (MMSE)[14] for the OSHPE population and the Mental Status Questionnaire (MSQ) for individuals enrolled in the TOUCH programme were used to measure cognitive functioning, and were used as potential confounders in the association between performance-based physical assessments and functional dependence.[15] Individuals with 23 or fewer points on the MMSE and three or more errors on the MSQ were considered to have cognitive impairment.[15 16]

Statistical analysis

Demographic and clinical variables were compared between the participants with and those without personal care using Student t tests for continuous variables and χ^2 tests for categorical variables. To compare the predictive ability of the study measures, receiver-operated characteristic (ROC) curves were inspected to determine cut-points for each test that best discriminated between the individuals with and those without personal care. Cut-points for maximising the sensitivity and specificity for each test were determined using the Youden index.[17] The area under the curve (AUC), sensitivity and specificity were then calculated for the cut-points. We used multivariate logistic regression analyses to determine ORs and 95% CIs, and to assess independent associations of the cut-points of physical performance measures for demand for personal care. The participants were divided into two groups according to the cut-point of the performance-based physical assessments. Covariates were added sequentially to the logistic model to evaluate the associations at different levels of adjustment. Model 1 included each performance-based physical assessment, and model 2 included the model 1 variables plus age, sex and cognitive impairment as determined by the MMSE or MSQ. Model 3 included all performance-based physical assessments plus age, sex and cognitive impairment. The participants were then divided into five groups as follows: individuals with no risk and those with 1, 2, 3 or 4 risks, according to the number of risks identified by the cut-points of the performance-based physical assessments. The ORs and 95% CIs for the number of risks were calculated adjusted for age, sex and cognitive impairment. All statistical contrasts were made at the 0.05 level of significance, and all data management and statistical computations were performed using the IBM SPSS Statistics V.19.0 software package (SPSS Inc, Chicago, Illinois, USA).

RESULTS

Comparison between participants with and those without personal care

Table 1 shows the characteristics of the participants. The participants with personal care were significantly older ($p<0.001$), included a higher number of women ($p<0.001$) and a higher number of persons with cognitive impairment ($p<0.001$) than those without personal care. For the comparison of performance-based assessments, the participants with personal care had significantly lower scores on all physical tests ($p<0.001$) compared

Table 1 Characteristics of the participants

	Participants with personal care (n=6791)	Participants without personal care (n=3560)
Age (years)*	82.6±6.7	71.8±5.2
Sex, women, n (%)*	4720 (69.5)	1793 (50.4)
Cognitive impairments, n (%)*	2962 (43.6)	562 (15.8) [8]
GS (kg)*	16.3±6.9	27.3±7.8
CST (s)*	13.0±5.6	8.6±2.4
CWS (m/s)*	0.7±0.3	1.2±0.2
TUG (s)*	16.6±7.7	8.9±1.8
Care level in the LTCI, n (%)		
Support need level 1	804 (11.8)	0 (0)
Support need level 2	1112 (16.4)	0 (0)
Care need level 1	2057 (30.3)	0 (0)
Care need level 2	1687 (24.8)	0 (0)
Care need level 3	842 (12.4)	0 (0)
Care need level 4	257 (3.8)	0 (0)
Care need level 5	32 (0.5)	0 (0)
Disability of basic ADLs, n (%)		
Eating	105 (1.5) [136]	0 (0)
Grooming	398 (5.9) [136]	0 (0)
Bathing	1374 (20.2) [136]	0 (0)
Locomotion	745 (11.0) [136]	0 (0)
Stairs	1508 (22.2) [136]	0 (0)

Individuals with 23 or fewer points on the MMSE in the participants without personal care and with three or more errors on the MSQ in the participants with personal care are considered to have cognitive impairment. Beneficiaries of the LTCI can use multiple services for which they are eligible, according to their care plan up to the maximum amount (£382 for Support Level 1; £800 for Support Level 2; £1275 for Care Level 1; £1498 for Care Level 2; £2058 for Care Level 3; £2354 for Care Level 4; £2756 for Care Level 5), in principle, for a 10% copayment and can use more services than covered as long as they pay all the costs for the services beyond the maximum level (calculated at £1=130 yen).
*Comparison between the participants with and without personal care; $p<0.001$, [ ] missing value.
CST, chair stand test; CWS, comfortable walking speed; GS, grip strength; LTCI, long-term care insurance; MMSE, mini-mental state examination; MSQ, mental status questionnaire; TUG, timed up-and-go test.

Table 2 Cut-points for the risk of demand for personal care and associated sensitivity, specificity, area under the curve (AUC), and OR statistics for all participants

	Criterion	Sensitivity	Specificity	AUC
GS (kg)				
Men	<26	74	89	0.88
Women	<17	80	88	0.90
CST (s)				
Men	≥10	72	74	0.79
Women	≥10	67	77	0.78
CWS (m/s)				
Men	<1.0	86	85	0.92
Women	<1.0	90	85	0.94
TUG (s)				
Men	≥11	76	88	0.88
Women	≥11	79	89	0.90

CST, chair stand test; CWS, comfortable walking speed; GS, grip strength; TUG, timed up-and-go test.

with those in participants without personal care (table 1). The number of participants with and without personal care who used the walking aid during the walking tests were 2593 (38.2%) and 35 (1.0%), respectively.

Cut-points between participants with and those without personal care

ROC curve analysis results, showing the performance cut-points for each test and associated statistics, are shown in table 2. The Youden index determined the cut-points for the demand for personal care as follows: GS in men and women was <26 and <17 kg, respectively; CST was ≥10 s, CWS was <1.0 m/s and TUG was ≥11 s for both sexes. The CWS score had the highest AUC for discriminating the demand for personal care and displayed good sensitivity and specificity (85–90%). High AUCs were also found for GS and TUG, as well as fair to good sensitivity and specificity (74–80%).

Relationships between cut-points and risk of disability

The multiple logistic regression models showed significant relationships between physical performances and the demand for personal care (table 3). The demand for personal care was most closely related to CWS in model 1 (OR=34.7; 95% CI 30.9 to 39.0). These results remained essentially unchanged after controlling for age, sex, cognitive impairment and other physical performance tests. In the final model (model 3), the highest OR of factors related to the demand for personal care was for CWS (OR=5.9; 95% CI 5.0 to 6.9). Figure 1 shows the distribution of CWS for participants with personal care. Participants who walked 1.1 m/s and faster had the lowest amount of personal care (20%). The rate of participants with personal care increased rapidly with a CWS slower than 1.1 m/s, and 90% of participants with a CWS slower than 0.8 m/s had personal care (figure 1A). The rate of functional decline increased rapidly for individuals walking slower than 1 m/s in women (figure 1C) rather than men (figure 1B), and with the rate of functional decline reaching 90% when CWS was slower than 0.8 m/s in both sexes (figure 1B,C).

There was a significant relationship between the number of risks based on the physical performance tests and the demand for personal care. The ORs and 95% CIs for personal care in participants with 1, 2, 3 and 4 risks were 3.1 (2.6 to 3.8), 10.6 (8.7 to 13.1), 35.6 (28.6 to 44.5) and 141.3 (103.6 to 192.7), respectively, compared with participants without risks (p<0.001). Figure 2 shows the distributions of the number of risks for demand for personal care. The rates of participants with personal care who had no risk, 1, 2 and 3 or more risks were 8.7%, 38.5%, 75.6% and 90.0%, respectively (figure 2).

DISCUSSION

Neuromuscular function, including muscle strength, balance and gait, and cognitive function are important risk factors for disability. Performance-based assessment of these factors can be used to identify people at an increased risk of future functional decline. We examined the use of various measures to identify the most useful measure for screening the demand for personal care.

Cut-points of demand for personal care

In the current study, univariate analyses identified all physical tests as being able to discriminate between participants with and those without personal care. When performance was dichotomised for cut-points, GS, CST, CWS and TUG retained statistically significant relationships with personal care. The CWS test (cut-point, 1 m/s) displayed the highest OR in the final model, with good sensitivity and specificity with respect to

Table 3 Relationships between physical performances and the demand for personal care

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
GS (men: <26 vs ≥26 kg, women: <17 vs ≥17 kg)	20.9 (18.6 to 23.5)*	8.5 (7.4 to 9.7)*	4.1 (3.5 to 4.8)*
CST (≥10 vs <10 s)	6.6 (6.1 to 7.3)*	4.1 (3.7 to 4.7)*	1.3 (1.1 to 1.5)*
CWS (<1 vs ≥1 m/s)	34.7 (30.9 to 39.0)*	17.5 (15.3 to 20.0)*	5.9 (5.0 to 6.9)*
TUG (≥11 vs <11 s)	27.1 (24.1 to 30.5)*	15.3 (13.4 to 17.6)*	4.0 (3.4 to 4.8)*

*p<0.01.

Model 1 was crude ORs and Model 2 was adjusted for age, sex and cognitive impairment. Model 3 was adjusted for age, sex, cognitive impairment and physical performances.

CST, chair stand test; CWS, comfortable walking speed; GS, grip strength; TUG, timed up-and-go test.

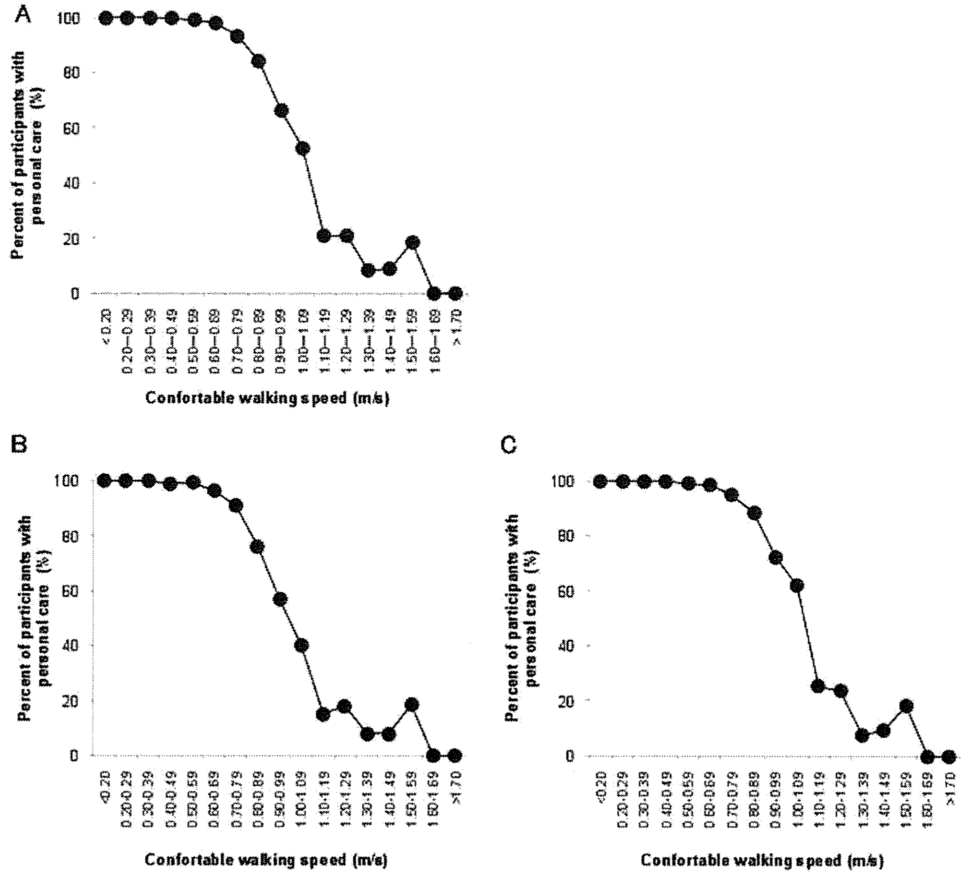

Figure 1 Comfortable walking speed distributions of participants with personal care in all participants (A), men (B) and women (C). The rate of participants with personal care markedly decreased at 1.0 m/s and faster at a comfortable walking speed.

identifying participants with personal care. At identified cut-points, GS (men, 26 kg; women, 17 kg), CST (10 s) and TUG (11 s) could also significantly discriminate participants with personal care with sensitivities and specificities of 67–89%. This result highlights what can occur when dichotomised rather than continuous data are used. There is an associated loss of information and reduced predictive accuracy as a trade-off for ease of scoring and test interpretation. These results, however, are consistent with previous findings that showed associations between measures of muscle strength and mobility and functional decline.[18]

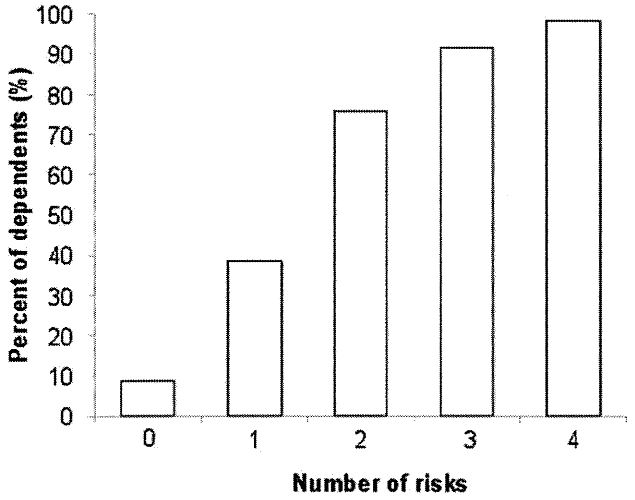

Figure 2 Participants with personal care according to the number of risks identified by cut-points of physical performance tests. Percentages of participants with personal care who had no risk, 1, 2 and 3 or more risks were 8.7%, 38.5%, 75.6% and 90%, respectively.

Gait speed and personal care

Gait velocity, as measured by the CWS test in this study, has been consistently reported to differentiate between participants with and those without personal care, with frail older persons walking significantly slower,[10 19] and has proved to be a strong predictor of adverse events, such as disability,[18 20–25] mortality,[21 22 26 27] hospitalisation[21 22 24 28] and falls.[28 29] Gait slowing, which occurs in the latest stages of life, suggests that mobility is so central to life that energy is shifted away from walking activity only when other vital activities are threatened,[30] which may lead to increased functional independence. In addition, a slower walking speed is an associated factor for subsequent dementia.[31] Dementia is one of the most important factors of health problems for functional decline in the aged population. For our study sample, the cut-point for CWS was 1 m/s, which is the critical point for future functional decline in community-dwelling older people determined by previous studies.[18 21 22 24 25] These results suggest that walking speed may be the most crucial measurement to determine the demand for personal care in older adults. Measurement of walking speed is reliable, valid, sensitive, inexpensive, safe, quick and a simple tool. Therefore, measurement of walking speed is suitable to use in community settings as a screening tool and evaluation for the effect of a care prevention programme.

Muscle strength and mobility and personal care

In the current study, higher ORs were found for GS and TUG, as well as CWS. Hand GS is an estimate of isometric strength in the upper extremity, but also correlates with strength in other muscle groups,[32] and therefore, is considered an estimate of the overall strength. In addition, GS has proved to be a strong predictor of physical functioning and disability,[33 34] morbidity[35] and mortality.[36 37] Our findings support previous evidence and add cut-points of <26 kg in men and <17 kg in women that discriminate those at high-risk for disability in community-living older people. The TUG has been recommended as a screening tool for identifying older people who are at risk for falling.[38 39] Bischoff *et al*[40] proposed a normative cut-point of 12 s for community-dwelling elderly people between 65 and 85 years of age. In daily clinical practice, elderly persons who perform the TUG in >12 s should receive early evaluation and intervention. Our results regarding TUG cut-points are in line with these previous studies.

Strengths and limitations

Strengths of the present study include a large sample size and we used performance-based assessment, which could determine actual physical capacity and predict subsequent physical disability in community-living older people. However, the present study has a number of limitations. One of the limitations is that we analysed cross-sectional data. Therefore, further investigation of the validity of these tests in predicting the risk of disability in older people using a prospective study design is recommended. Another limitation is that many frail older people using healthcare services cannot walk because they have multiple diseases or geriatric syndromes. Non-ambulatory participants were excluded from our study. Therefore, we acknowledge that the study findings may not be generalised to this frailer group.

CONCLUSIONS

This study provides preliminary evidence that clinical tests of physical performances can predict the risk of disability in older people. Logistic regression analysis selected CWS as the best independent correlate of disability, with good sensitivity and specificity. Further investigation is required, and future research should include a prospective measurement of the risk of disability to more accurately determine the validity of screening tests for this population.

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