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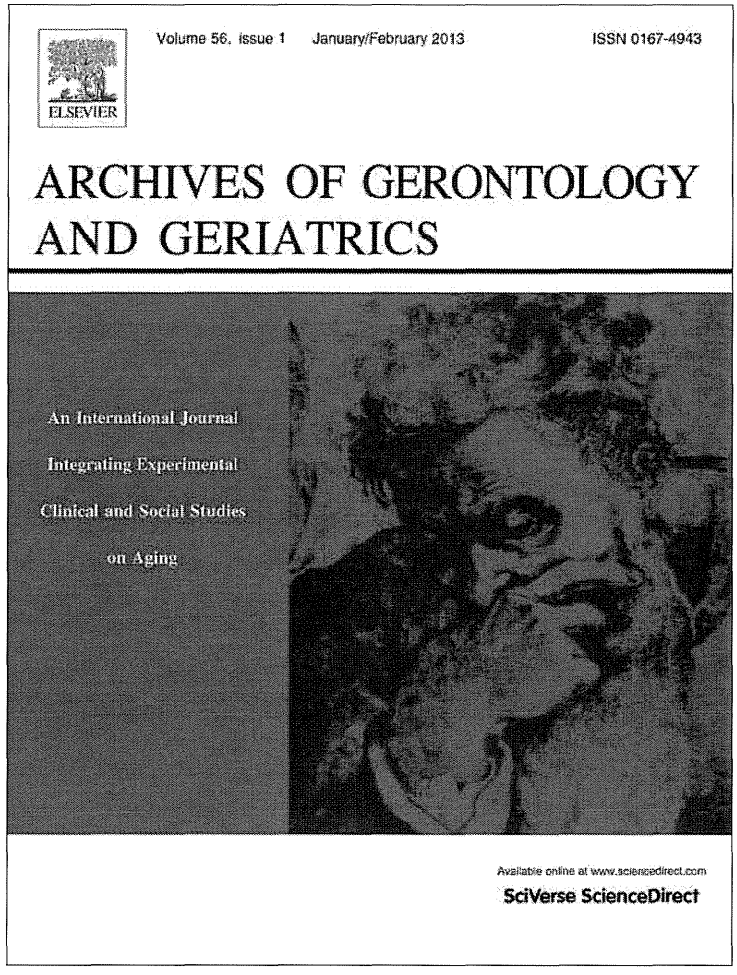

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# Relationship between going outdoors daily and activation of the prefrontal cortex during verbal fluency tasks (VFTs) among older adults: A near-infrared spectroscopy study

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ABSTRACT

This study sought to investigate the relationship between going outdoor daily and prefrontal cortex activation during execution of the VFT using near-infrared spectroscopy (NIRS) in community-dwelling older adults. Blood oxygenation changes in left and right prefrontal cortices were measured in twenty older adults (mean age 76.1 ± 6.7 years) by NIRS during VFT performance. In this task, participants were required to pronounce as many nouns as possible beginning with the letters "*Shi*," "*I*," and "*Re*." Changes in oxygenated hemoglobin (oxy-Hb) levels during the VFT were compared between two groups defined by the frequency of going outdoors: daily or non-daily within a week. Participants in both groups exhibited significantly increased oxy-Hb levels in the left and right prefrontal cortices during the VFT compared to a resting baseline condition. After controlling for age and gender, there were significant group-by-condition interactions on oxy-Hb levels with less activation during the execution of the VFT over both cortices in the non-daily group (left: $F = 4.76$, $p = 0.04$; right: $F = 6.32$, $p = 0.02$). These findings indicate that going outdoors daily is associated with increased activation in the prefrontal cortices during VFT performance in community-dwelling older adults.



## 1. Introduction

For older people, getting outdoors requires a certain level of physical and cognitive functioning. A low frequency of going out has been found to predict functional and intellectual decline among frail older adults, whereas going out frequently corresponded with improvement of baseline self-efficacy for both daily activities and health promotion (Kono, Kai, Sakato, & Rubenstein, 2004). In a recent longitudinal study, with a mean follow-up of 4.4 years, constricted living space was found to lead to decreased physical activity and social engagement, and was associated with increased risk of Alzheimer disease (AD), mild cognitive impairment (MCI), and a faster rate of global cognitive decline among older adults (James, Boyle, Buchman, Barnes, & Bennett, 2011). Thus, going out into the life-space seems to play an important role in maintaining physical and cognitive function among older adults.

Older adults with cognitive impairment, such as AD patients, demonstrate diminished activation of the prefrontal cortex during cognitive tasks compared to those who are cognitively healthy (Herrmann, Langer, Jacob, Ehlis, & Fallgatter, 2008; Li, Zheng, Wang, & Gui, 2009; Richter, Herrmann, Ehlis, Plichta, & Fallgatter, 2007). Cognitive decline is thought to be a consequence of neurodegeneration in the brain, and abnormal activation during cognitive task performance has been found to precede decline of cognitive function (Clark et al., 2012; O'Brien et al., 2010). A previous functional neuroimaging study used near-infrared spectroscopy (NIRS) to investigate the oxygenation of brain tissue during the VFT in dementia patients (Herrmann et al., 2008). The results revealed that dementia patients exhibited reduced brain activation during VFT performance, as indicated by significantly lower oxygenated hemoglobin (oxy-Hb) levels compared to control subjects. The VFT is a neuropsychological task with category-fluency and letter-fluency versions. The VFT allows an

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assessment of a subject's ability to retrieve a series of nouns based on a common criterion. Performance in the VFT has been found to decline according to cognitive dysfunction, and VFT is one of the most effective neuropsychological tests to assess the risk of AD (Laws, Duncan, & Gale, 2010). The frontal lobe is essential for a range of important cognitive functions, including executive function and memory. In particular, performance in the letter version of the VFT is thought to be closely associated with frontal lobe function (Herrmann, Ehlis, & Fallgatter, 2003; Kitabayashi et al., 2001). Decreased neural activation may be a suitable predictor for the risk of cognitive decline.

Going outdoors daily is beneficial for older people, and is correlated with reduced functional decline (Jacobs et al., 2008). However, the influence of frequently going outdoors on brain activation during cognitive tasks is unknown. An increased outdoor activity, such as walking, recreation, and sport, is associated with slower age-related cognitive decline and brain atrophy in older people (Erickson et al., 2010; Yaffe, Barnes, Nevitt, Lui, & Covinsky, 2001). Therefore, we hypothesized that the frequency of going outdoors may be related to age-related decline of brain activation. We aimed to test the hypothesis that going outdoors daily would exert positive effects on functional brain activation during performance of the letter version of the VFT among older adults.

## 2. Subjects and methods

### 2.1. Subjects

Twenty right-handed older adults (10 females; aged 66–89 years) living independently in the community participated in this study after giving written informed consent. None of the participants had a previous history of major psychiatric illness (e.g., schizophrenia or bipolar disorder), other serious neurological or musculoskeletal diagnoses, or clinical depression. We also excluded participants if they had a diagnosis of dementia, exhibited moderate to severe cognitive decline, were taking anti-Alzheimer's drugs, or required long-term care. This study was approved by the ethics committee of the National Center for Geriatrics and Gerontology.

### 2.2. Frequency of going outdoors

The frequency of going outdoors was assessed using a sub question item of the life-space assessment scale (Baker, Bodner, & Allman, 2003), which asked participants whether they had been to places in their neighborhood, and within their town during the past four weeks. The available responses were daily, four to six times a week, one to three times a week, less than once a week, or none. Participants were classified into the daily ($n = 7$) and non-daily ($n = 13$) groups based on their responses.

### 2.3. Other variables

Functional capacity was measured using the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC), a self-report questionnaire (Koyano, Shibata, Nakazato, Haga, & Suyama, 1991). The TMIG-IC is a multi-dimensional 13-item index developed to assess the functional capacity of older people with intact activities of daily living according to their abilities in complex activities. The total score on this index ranges from 0 to 13 points, with higher scores indicating higher functional capacity. General cognitive function was examined using the Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975). The MMSE was assessed by licensed and experienced clinical speech therapists.

### 2.4. Verbal-fluency task and procedure

For the letter version of the VFT, we used a block design with three 140-s blocks consisting of a 10-s pre-resting period, a 60-s activation period, and a 70-s post-resting period (Fig. 1). We began recording after fitting the montage of sensors to determine whether they were placed correctly, without artifacts. Participants were then told to relax with their eyes open and fixate on a circle displayed in front of them. When participants seemed to be relaxed, a baseline measurement of 10 s was conducted. In the phonemic VFT task, the participant was instructed to retrieve as many words as possible beginning with the Japanese syllabic characters (hiragana) "*Shi*," "*I*" and "*Re*," respectively, in a 60-s period (Takahashi et al., 2008). Each of these three conditions (different starting letters) lasted 60 s. There was a 70-s post-resting period after each 60-s activation period during each VFT.

### 2.5. NIRS measurements

Changes in oxy-Hb levels were recorded using the Spectratech OEG-16 system (Spectratech Inc., Yokohama, Japan) with 16 channels. The NIRS system used two wavelengths (approximately 770 and 840 nm) of near-infrared light, and absorption was

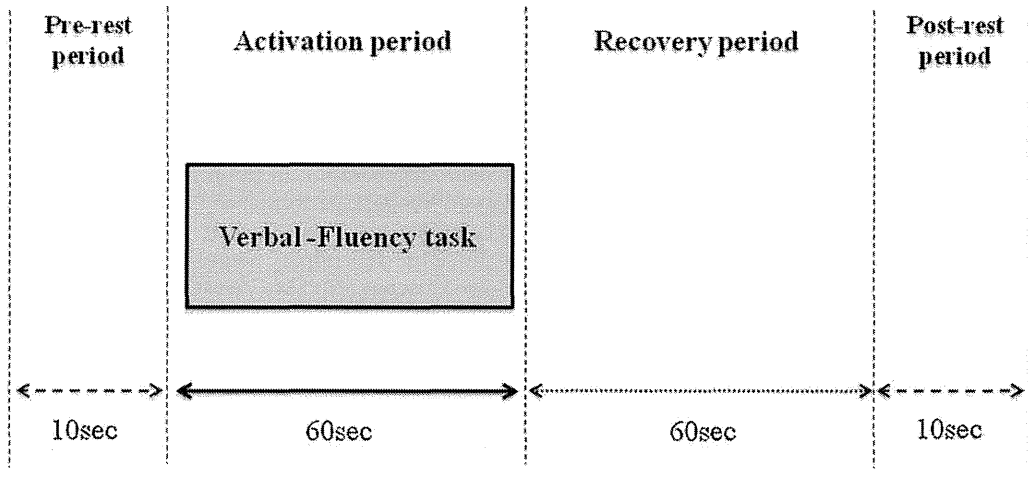


**Fig. 1.** Time course of one block. Total time of one block is 140 s. Each block contained a 10-s pre-resting period, a 60-s activation period, and a 70-s post-resting period. NIRS data were collected in three blocks (beginning with the Japanese syllabic characters "*Shi*," "*I*" and "*Re*," respectively).

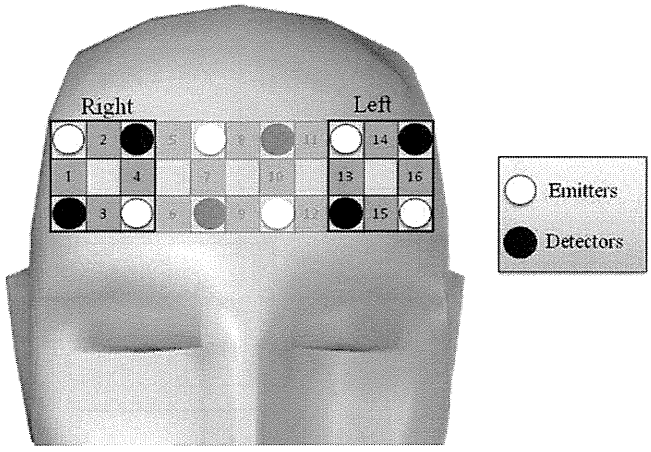


**Fig. 2.** Location of NIRS probes and channels. The NIRS system in this study consisted of six light sources (white) and six detector fibers (black), resulting in 16 channels of source-detector pairs. nROIs were arranged into two regions: RIFG (channels 1, 2, 3, and 4), and LIFG (channels 13, 14, 15, and 16).

recorded to estimate oxy-Hb levels. The temporal resolution was set at 650 ms. The emission probes were located 3.0 cm apart from the detector probes. This system could measure changes in oxy-Hb levels at a depth of approximately 3 cm below the scalp. Six emission and six detector probes were arranged in a 6 (wide) × 2 (long) matrix on the participant's forehead. Thus, cortical responses were obtained from a total of 16 locations. The center of the probe matrix was placed on Fpz (midpoint between Fp1 and Fp2) in accordance with the international 10/20 system used in electroencephalography. In this study, we analyzed NIRS data for the following measurement points, which were labeled as Ch1–4 for right frontal channels and Ch13–16 for left frontal channels, approximately covering the anterior and ventrolateral prefrontal cortices (Fig. 2).

### 2.6. Data analysis

Student's *t* tests and chi-square tests (to test for gender differences) were used to compare demographic characteristics between the daily and non-daily groups. For the NIRS data, a low-pass filter was set at 0.05 Hz using a fast Fourier transform (FFT) to exclude artifacts caused by minor movements of the participant, and a baseline correction was performed using linear fitting based on two baseline data: the mean across a 10-s-period just before the VFT section, and the mean across a final 10-s period of 70 s after the VFT section (Fig. 1). To determine oxy-Hb levels in the specific region of the lateral prefrontal cortex related to changes of activation during the VFT (Kameyama, Fukuda, Uehara, & Mikuni, 2004; Kameyama et al., 2006; Suto, Fukuda, Ito, Uehara, & Mikuni, 2004), regions of interest for NIRS data (nROIs) were arranged into two regions: (1) right inferior frontal gyrus (RIFG: channels 1, 2, 3, and 4); and (2) left inferior frontal gyrus (LIFG: channels 13, 14, 15, and 16) (Fig. 2) (Kita et al., 2011). Changes in oxy-Hb levels in each nROI were averaged in each participant. NIRS data were compared between the daily and non-daily groups defined by the frequency of going outdoors. The delta oxy-Hb levels during the execution of the VFT were expressed relative to that during the rest condition in each nROI, and were compared between groups using student's *t* tests. A repeated-measures analysis of covariance (ANCOVA) model adjusted for age and gender was used to evaluate group differences on changes in oxy-Hb levels during the VFT. Post hoc analyses were conducted using Bonferroni comparisons to compare oxy-Hb levels between resting and VFT conditions in each group. Statistical analyses were performed using SPSS for Windows, version 19.0 (SPSS, Chicago, IL, USA). Statistical significance was set at 0.05 for all analyses.

## 3. Results

Table 1 summarizes the characteristics of the daily and non-daily groups. There were no significant between-group differences in the characteristics, TMIG-IC, MMSE, and VFT performance. During the VFT, we found a significant increase of oxy-Hb levels over both inferior frontal gyri compared to a resting baseline condition in the daily (RIFG: baseline, $-0.004 \pm 0.008$ mM mm; VFT, $0.258 \pm 0.234$ mM mm, $p = 0.03$; LIFG: baseline, $-0.001 \pm 0.005$ mM mm; VFT, $0.275 \pm 0.256$ mM mm, $p = 0.02$) and non-daily (RIFG: baseline, $0.001 \pm 0.003$ mM mm; VFT, $0.087 \pm 0.091$ mM mm, $p < 0.01$; LIFG: baseline, $0.000 \pm 0.006$ mM mm; VFT, $0.094 \pm 0.122$ mM mm, $p = 0.02$) groups. The delta oxy-Hb of LIFG in the daily group was significantly higher than that in the non-daily group in the RIFG (daily, $0.262 \pm 0.233$ mM mm; non-daily, $0.086 \pm 0.091$ mM mm, $p = 0.03$) and LIFG (daily, $0.276 \pm 0.253$ mM mm; non-daily, $0.093 \pm 0.119$ mM mm, $p = 0.04$) (Fig. 3). In both inferior frontal gyri, there was a significant group-by-condition interaction on oxy-Hb levels, with higher levels in the daily group (RIFG: $F = 6.32$, $p = 0.02$; LIFG: $F = 4.76$, $p = 0.04$) even after adjusting for age and gender.

## 4. Discussion

The current results indicate that going outdoors daily is associated with activation in the prefrontal cortices. Subjects who go outdoors daily exhibited greater activation in the prefrontal cortices during the execution VFT performance compared to subjects who do not. These findings suggest that going outdoors may contribute to successful oxygenation during the performance of cognitive tasks.

The frequency of going outdoors is a component of the life-space and could be a useful and simple indicator for predicting changes in functional capacity among older adults (Kono et al., 2004), and walking outside the home is important for maintaining functional independence in frail older adults (Shimada et al., 2010; Simonsick, Guralnik, Volpato, Balfour, & Fried, 2005). Previous findings indicate that functional level is related to the frequency of going outside in older adults, especially frail older people (Ganguli, Fox, Gilby, & Belle, 1996; Kono & Kanagawa, 2001). Several longitudinal studies (Fujita, Fujiwara, Chaves, Motohashi, &

**Table 1**
Participant characteristics.

| | All participants ($n = 20$) | Daily ($n = 7$) | Non-daily ($n = 13$) | $p$ |
|---|---|---|---|---|
| Age, years | 76.1 ± 6.7 | 75.6 ± 7.0 | 76.3 ± 7.0 | 0.83 |
| Sex, %female | 50.0 | 42.9 | 53.8 | 0.63 |
| Body mass index, kg/m$^2$ | 24.0 ± 3.0 | 25.0 ± 3.3 | 23.5 ± 2.8 | 0.30 |
| Education, years | 10.7 ± 2.6 | 11.3 ± 2.4 | 10.3 ± 2.7 | 0.43 |
| TMIG, score | 12.2 ± 0.9 | 12.4 ± 0.8 | 12.0 ± 1.0 | 0.34 |
| MMSE, score | 26.1 ± 2.6 | 27.0 ± 2.8 | 25.6 ± 2.5 | 0.24 |

*Note*: Data are presented as mean ± SD, unless otherwise indicated.

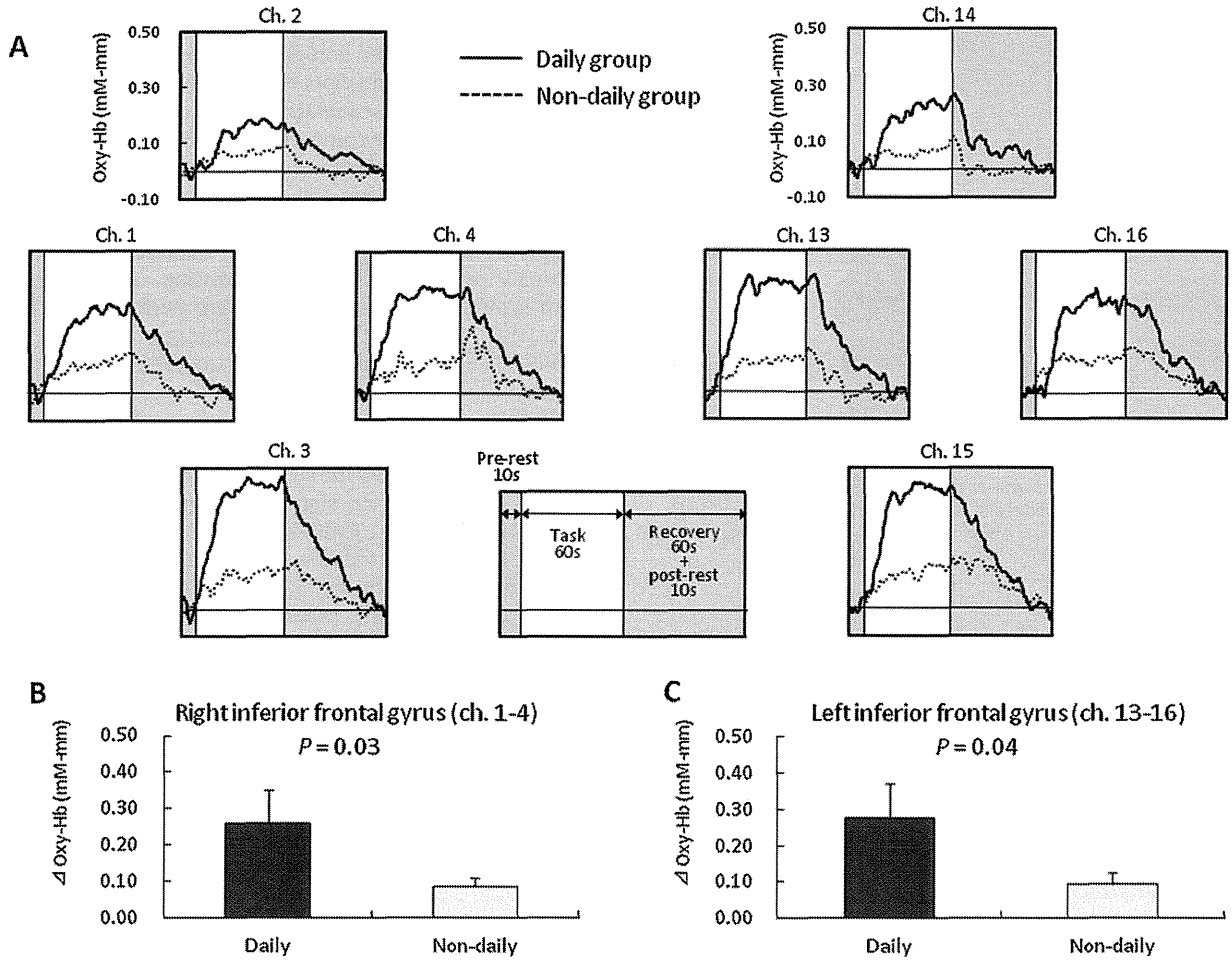


**Fig. 3.** Oxy-Hb values averaged for the daily (solid line) and non-daily (dotted line) groups for the RIFG (channels 1, 2, 3, and 4) and LIFG (channels 13, 14, 15, and 16) (A). Comparisons of the delta oxy-Hb (changes of oxy-Hb levels during the execution of the VFT compared with the rest condition) between the daily and non-daily groups in the RIFG (B) and the LIFG (C). Error bars represent 1 SE.

Shinkai, 2006; James et al., 2011) have indicated that a low frequency of going out predicts functional decline, even when there are no differences on physical and cognitive function at baseline. In the current study, all participants were living independently in the community with relatively good health status, and there were no differences in functional capacity and general cognitive function between the daily and non-daily groups. VFT performance did not differ between the groups. However, there was a significant group-by-condition interaction in oxy-Hb levels, with higher levels in the daily group VFT performance. These results indicate that going outdoors daily might have a positive effect on brain activation, despite some specific differences in the VFT performance. Reduced brain activation during cognitive tasks may be associated with functional decline in the future as well as a lower frequency of going outside. The current cross-sectional study is not able to answer these questions conclusively.

Rosano et al. investigated the relationship between physical activity and brain activation using functional magnetic resonance imaging (fMRI) during cognitive tasks requiring the prefrontal lobe (i.e., digit symbol substitution test). The researchers suggested that engagement in physical activity increased task-induced activation and had beneficial effects on cognitive health (Rosano et al., 2010). Indeed, recent longitudinal studies suggest that reduced life-space is related to future cognitive decline and increased risk of AD and MCI among community-dwelling older adults (Crowe et al., 2008; James et al., 2011). Frequency of attainment is included as an important factor for assessing life-space (Baker et al., 2003). A previous study indicated that greater activity levels in youth reduced the risk of cognitive impairments in aging, and that involvement in certain activities may contribute to cognitive "reserve" (Fritsch et al., 2005). In addition, an epidemiological study suggested that participation in cognitively stimulating leisure activity (e.g., attending a class, lecture, or public meeting; and participating in community, church, or social clubs) may attenuate the effects of brain lesion pathology on cognitive performance in older adults (Saczynski et al., 2008). Taken together, these findings indicate that maintaining a high frequency of outdoor activities, consequently extending the life-space, could have positive effects on brain health, preventing future cognitive decline among independent older adults.

Previous studies using NIRS have investigated the functional brain oxygenation correlates of locomotion (Holtzer et al., 2011; Miyai et al., 2001; Suzuki, Miyai, Ono, & Kubota, 2008). These studies have revealed that walking itself is associated with oxy-Hb levels in the prefrontal, primary sensorimotor, and supplementary motor areas (Holtzer et al., 2011; Miyai et al., 2001). A recent NIRS study provided surprising evidence that moderate exercise immediately increased both cognitive performance and dorsolateral prefrontal activation while executing cognitive tasks (Yanagisawa et al., 2010). These results suggest that physical activity itself may increase brain oxygenation in the frontal region, and have beneficial effects on cognitive health. Moreover, increased oxy-Hb levels in the prefrontal cortex during walking while talking

were found to be greater than normal walking in both young and old individuals (Holtzer et al., 2011). In daily life, multi-task conditions are common while performing outdoor activities. To produce appropriate behavior in these situations, older adults require significantly more overall attentional resources as the difficulty of locomotion is increased compared to young adults (Lajoie, Teasdale, Bard, & Fleury, 1993; Sparrow, Bradshaw, Lamoureux, & Tirosh, 2002). Frequently going outdoors may require an increased attentional capacity for locomotor tasks, and exerting positive effects on brain activation among older adults.

Furthermore, going outdoors more frequently may also enhance a person's engagement in social interaction and activity. For example, engaging in conversation with other people is a common activity in the daily lives of most people. A previous study using NIRS reported that the frontal and superior temporal regions were activated during face-to-face conversation, with stronger activity during speaking segments in a conversation (Suda et al., 2010). Outdoor activities including walking under multi-task conditions and meeting other people and engaging in face-to-face conversation may increase brain activation, particularly in the prefrontal cortex, among older adults.

Some methodological limitations of this study should be considered. Our investigation was conducted under experimental conditions, and used a cross-sectional design. We classified participants into daily and non-daily groups based on their responses to a sub-question item of the life-space assessment scale. The group sizes were small and a relevant frequency of going outdoors was unclear. Future studies including a large sample size, longitudinal design, and regression analyses may be needed to further clarify the relationship between the frequency of going outdoors and brain activation among older adults. Despite these limitations, the results indicate that going outdoors, frequent walking, and increased physical activity are likely to be beneficial for preventing age-related decline in brain activations. Future longitudinal studies should investigate whether going outdoors has a causal role on brain health in older adults. A second limitation is that our NIRS probes only recorded from the frontal area, particularly the prefrontal cortices, meaning that the activation of other cortical areas and deep brain structures was not observed. Gait requires complex visuo-sensorimotor coordination and is associated with activation of the medial frontoparietal region, e.g., the primary sensory and motor areas, supplementary motor area, lateral premotor cortex, cingulate cortex, superior parietal lobule, precuneus, and the infratentorial region including the dorsal (Fukuyama et al., 1997; Hanakawa et al., 1999; la Fougere et al., 2010). Future research should examine the relationship between the activation of other cortical areas and the frequency of going outdoors, and should use other neuroimaging techniques (e.g., positron emission tomography, single photon emission tomography, and fMRI) to further investigate whether going outdoors daily is a beneficial behavior for neural health among the aged population. In addition, the current study included no measure of physical activity, such as a self-report inventory or a pedometer, so we were unable to accurately quantify the amount of exercise undertaken. Furthermore, the sample size of the current cross-sectional study was relatively small, limiting the generalizability of the results. Further experiments using longitudinal and interventional designs will be required for more rigorously defining the effect of going outdoors daily on aging in the brain.

## 5. Conclusion

Older adults in both the going outdoors daily and non-daily groups exhibited significantly increased oxy-Hb levels in the left and right prefrontal cortices during VFT performance compared to a resting baseline condition. After controlling for age and gender, there were significant group-by-condition interactions on oxy-Hb levels, with less activation during VFT performance over both cortices in the non-daily group. These findings demonstrated that going outdoors daily was associated with increased activation in the prefrontal cortices during VFT performance in community-dwelling older adults.

## Conflict of interest statement

None.

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ORIGINAL ARTICLE

# Factors associated with life-space in older adults with amnestic mild cognitive impairment

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**Aim:** Restriction of life-space is associated with physical performance and functional decline in older adults. Little is known about the factors associated with life-space in older adults with amnestic mild cognitive impairment (aMCI). The purpose of this study was to identify factors associated with life-space in older adults with aMCI.

**Methods:** The study participants were 69 older adults (mean age 74.5 years, males 56.5%) who were identified with aMCI. Life-space mobility was measured using a Japanese translation of the life-space assessment (LSA). Age, sex, cognitive function (general function, executive function and processing speed), physical performance, instrumental activities of daily living status (IADL) and fear of falling (FoF) were measured as potential relevant factors.

**Results:** Univariate analysis showed that the LSA was associated with FoF, sex, physical performance, processing speed and IADL. In the stepwise regression analysis, FoF, processing speed and IADL maintained a significant association with the LSA scores, although sex and physical performance did not reach significance.

**Conclusion:** The results suggest that the restrictions of life-space in older adults with aMCI were more affected by the FoF, slower processing speed and restricted IADL than sex or physical performance. **Geriatr Gerontol Int 2012; ••: ••–••.**

**Keywords:** community-dwelling elderly population, fear of falling, information processing, life-space, mild cognitive impairment.

## Introduction

Mild cognitive impairment (MCI) is widely regarded as a transitional syndrome between normal cognitive aging and clinical dementia.[1] This is particularly the case for amnestic MCI (aMCI), which is likely to progress to Alzheimer's disease (AD).[2–4] The diagnostic criteria show that people with MCI have "generally" intact activities of daily living (ADL), although investigations of instrumental activities of daily living (IADL) have shown marginal limitations for older adults with MCI.[5–8] Furthermore, older adults with cognitive deficits suggestive of MCI have shown lower mobility, including reduced life-space, driving space and driving frequency, as well as increased driving difficulty compared with cognitively normal individuals.[9]

Life-space is the spatial extent of a person's mobility. It has been conceptualized as a series of concentric zones, ranging from one's bedroom to one's region of the country.[10] Xue *et al.* reported that a slightly constricted life-space (going into the neighbourhood less

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than four times a week) was an important risk factor for the development of frailty, whereas a severely constricted life-space (i.e. never leaving home) indicated a high risk of mortality.[11] A lower fluency of going outdoors (less than once a week) was associated with a limitation in basic ADL and IADL.[12] Thus, an extended life-space seems to play an important role in maintaining health and function in older adults.

Life-space assessment (LSA) was developed to evaluate mobility status by measuring the life-space for elderly individuals living in a community.[13] The LSA may indirectly reflect the physical activity status of older adults because the LSA score is associated with physical performance, ADL and sociodemographic factors.[14] Baker *et al.*[13] suggested that the LSA is sensitive to marginal limitations before older persons experience difficulties in performing ADL or IADL. Older adults with MCI restrict their life-space,[9] and the LSA might be an early marker of functional decline in older adults with MCI. Furthermore, identifying the determinants of life-space is required to identify appropriate therapeutic strategies. According to previous studies among older adults, it has been reported that life-space is larger if they have better physical performance, cognitive function,[15] mental health and IADL functions,[13,16,17] and they are male.[16] However, it is not clear whether factors, such as demographic, physical and cognitive performance, and psychological status, are associated with life-space in older adults with MCI. We focused on aMCI (memory impairment), which is likely to progress to AD.[2–4] The purpose of the present study was to identify the determinants of life-space in older adults with aMCI.

## Methods

### *Participants*

The participants were recruited from two volunteer databases ($n = 1543$), which included elderly participants aged 65 years and over who either attended a health check in Obu, Japan, or were selected by stratified random sampling. Figure 1 shows the flowchart of participant recruitment and screening. The strata used in stratified random sampling were age and sex. In the first eligibility assessment for the present study, 528 potential participants who had either a Clinical Dementia Rating of 0.5 or memory complaints were enrolled. A total of 135 participants responded to the second eligibility assessment; 76 participants completed the assessment and met the inclusion criteria. The inclusion criteria required that they live independently in the community, speak Japanese, have adequate hearing and visual acuity, and be able to participate in the examinations, and met the definition of aMCI. In the present study, aMCI was defined according to Peterson's internationally-accepted criteria:[1] having memory complaints and an objective memory impairment,

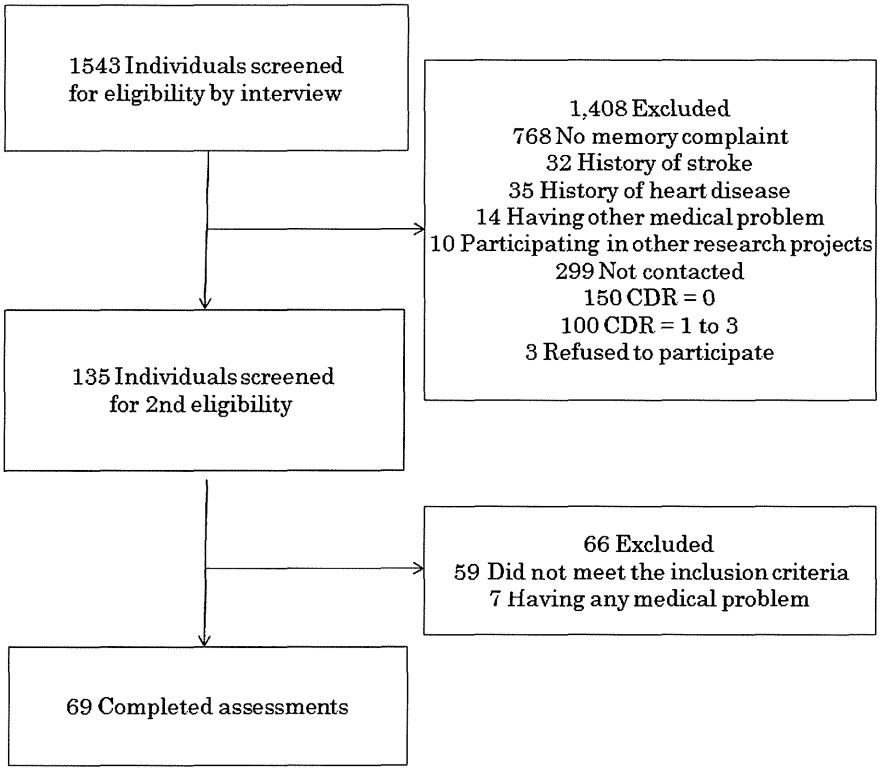


**Figure 1** Flow chart of participant recruitment and screening. CDR, Clinical Dementia Rating.

maintaining independent activities of daily living, preserved general cognitive function and no dementia. The objective memory impairment was defined as a lower score on the Wechsler Memory Scale-Revised (WMS-R) Logical Memory II.[18] The cut-off score to define the aMCI was adjusted by educational history (0–9 years: <7 points, 10–15 years: <10 points, more than 16 years: <12 points).[19] In addition, general cognitive function was found to be intact in all the 76 participants whose Mini-Mental State Examination (MMSE) scores were in the range of 24–30.[20] Seven participants were excluded based on the exclusion criteria, specifically a history of major psychiatric illness, other serious neurological or musculoskeletal diagnoses, or depression (Geriatric Depression Scale [GDS] scores greater than or equal to 10[21]). There were 69 older adults in the final analyzed sample ($n = 69$, age $M = 75.4$, proportion of males 56.5%, educational history $M = 11.0$). Written informed consent was obtained from the participants in accordance with the guidelines approved by the National Center for Geriatrics and Gerontology, and the Declaration of Human Rights, Helsinki, 1975.

### *Measurements*

Demographic data were recorded including age, sex and educational history. Life-space mobility was measured using a Japanese translation of the LSA.[13,22] The repeated forward–backward translation procedure was used to produce a Japanese version of the LSA. The translation was carried out by a native English translator and three Japanese translators, and confirmed by Baker *et al.*, a developer of the LSA. The LSA can be used to derive a score based on the reported movement distance for the 4 weeks preceding the assessment. The life-space levels ranged from the room where a person sleeps to beyond the person's town (five life-space levels): (i) "other rooms of your home besides the room where you sleep"; (ii) "an area outside your home, such as your porch, deck, or patio, hallway (of an apartment building) or garage, in your own yard or driveway"; (iii) "places in your neighbourhood other than your own yard or apartment building"; (iv) "places outside your neighbourhood, but within your town"; and (v) "places outside your town." For each life-space level, participants were asked how often they travelled to that area (less than once a week, 1–3 times each week, 4–6 times each week, daily) and whether they required assistance from another person or from an assistive device ("yes" or "no"). The LSA scores ranged from 0 ("totally room-bound") to 120 ("travelled out of town every day without assistance"), with lower scores reflecting lower life-space mobility.

All neuropsychological tests were carried out by well-trained speech therapists, and each score was rechecked by a single therapist blind to the other participant data. General cognitive function was evaluated using the Alzheimer's Disease Assessment Scale (ADAS).[23] The ADAS was designed specifically to evaluate cognitive and behavioural dysfunctions characteristic of AD.

Executive function was assessed using the Trail Making Test forms B (TMT-B).[24] Participants were required to navigate a series of alternating numbers and letters, and connect them in alternating sequential order. The time required to complete each task was recorded, with more time indicating worse performance.

Processing speed was assessed by using a version of the Digit Symbol-Coding (DSC) subtest of the Wechsler Adult Intelligence Scale III.[25] In the test, participants copied symbols that were paired with numbers. Using the key provided at the top of the exercise form, the participant drew the symbol under the corresponding number. The DSC score was the number of correct symbols drawn within 120 s.

The Timed Up & Go Test (TUG) was used to assess physical performance.[26] The TUG involves rising from a chair, walking 3 m, turning around, walking back to the chair and sitting down. Participants were instructed to complete the task at their usual pace. The score represented the time in seconds that the participant required to complete the assessment. Lower times indicate better balancing ability. The recorded TUG score was the lesser of the times measured in the two trials.

IADL were measured by the five-item subscale of Instrumental Self-Maintenance of the Tokyo Metropolitan Institute of Gerontology-Index of Competence (TMIG-IC), which has been shown to be reliable.[27] The IADL subscale of the TMIG-IC consisted of the following items: (i) "Can you use public transportation (bus or train) by yourself?"; (ii) "Are you able to shop for daily necessities?"; (iii) "Are you able to prepare meals by yourself?"; (iv) "Are you able to pay bills?"; and (v) "Can you handle your own banking?" Participants were asked about the competence status of the implementation of each item. The response to each item in the index was designated as "yes" (able to do, 1 point) or "no" (unable to do, 0 point). The total score of the IADL subscale ranges from 0 (limitation of IADL) to 5 (high level of IADL).

Fear of falling (FoF) was measured as a psychological factor causing activity restriction. The FoF refers to the lack of self-confidence that normal activities can be carried out without falling.[28] The FoF was assessed using a closed-ended question: "Are you afraid of falling now?" Participants responded by selecting one item from an ordered set of choices. Participants who responded "somewhat" or "very much" were assigned to the fear group; participants who responded "a little" or "not at all" were assigned to the no-fear group.[29]

### *Statistical analysis*

The relationships between the LSA and the other measurements were examined using Pearson's correlations. Spearman's correlations were used to examine the relationship among ordinal variables; that is, IADL. Unpaired *t*-tests were used to compare the LSA scores for categorical variables; that is, sex and the FoF.

A multivariate linear regression model was used to examine whether the potential determinants were associated independently with the LSA score. Independent variables included age, sex, the ADAS, DSC, TMT-B, TUG, IADL and FoF scores. Sex and FoF were used as dummy variables (male = 0, female = 1; no fear = 0, fear = 1). Statistical analyses were carried out using the SPSS version 11.0 software package (SPSS, Chicago, IL, USA), with $P < 0.05$ accepted as significant.

## Results

Table 1 shows the demographic and clinical characteristics of study participants. In the correlation analysis, the LSA scores had modest correlations with TUG ($r = -0.342$, $P = 0.004$), DSC ($r = 0.365$, $P = 0.002$) and IADL ($r = 0.254$, $P = 0.035$). The LSA was not correlated with age ($r = -0.164$, $P = 0.18$), ADAS ($r = -0.07$, $P = 0.53$) or TMT-B ($r = -0.21$, $P = 0.08$). Males had significantly higher LSA scores than females (males 102.3 ± 19.7, females 88.7 ± 17.8; $P = 0.004$). The no-fear group had significantly higher LSA scores than the fear group (non-fear 104.3 ± 19.7, fear 88.7 ± 17.8; $P < 0.001$).

**Table 1** Demographic and clinical characteristics of study participants

| | Participants ($n = 69$) |
|---|---|
| Age (years) | 75.4 ± 6.9 (69–94) |
| Education (years) | 11.0 ± 2.6 |
| Sex (males) | 39 (56.5) |
| MMSE (points) | 26.8 ± 1.8 |
| GDS (points) | 3.0 ± 2.0 |
| LSA (points) | 96.3 ± 19.9 |
| ADAS (points) | 6.4 ± 2.2 |
| DSC (points) | 45.7 ± 14.7 |
| TMT-B (s) | 204.5 ± 109.1 |
| TUG (s) | 9.2 ± 2.3 |
| IADL (points) | 4.9 ± 0.2 |
| FoF (the fear group) | 31 (44.9) |

Values are presented as mean ± SD or n (%). ADAS, Alzheimer's Disease Assessment Scale; DSC, Digit Symbol-Coding subtest of the Wechsler Adult Intelligence Scale III; FoF, Fear of Falling; GDS, Geriatric Depression Scale; IADL, Instrumental Activities of Daily Living subscale of TMIG-IC; LSA, Life-Space Assessment; MMSE, Mini-Mental State Examination; TMT-B, Trail Making Test forms B; TUG, Timed Up & Go Test.

**Table 2** Factors associated with a larger life-space in stepwise multiple regression

| | Factors | β | *P* | $R^2$ |
|---|---|---|---|---|
| LSA | FoF | −0.370 | 0.000 | 0.37 |
| | DSC | 0.278 | 0.007 | |
| | IADL | 0.274 | 0.008 | |

DSC, Digit Symbol-Coding subtest of the Wechsler Adult Intelligence Scale III; FoF, Fear of Falling; IADL, Instrumental Activities of Daily Living subscale of TMIG-IC; TUG, Timed Up & Go Test.

Table 2 shows the factors significantly related to LSA scores in the stepwise multiple regression. The stepwise method was used to empirically determine the best combination of the demographic, cognitive, physical and psychological factors to account for the LSA scores. The model explained 37% of the LSA score variance. Factors retained in the final model were the FoF ($\beta = -0.37$, $P = 0.001$), DSC ($\beta = 0.278$, $P = 0.007$) and IADL ($\beta = 0.274$, $P = 0.008$). The excluded variables in the model were age, sex, ADAS, TMT-B and TUG.

## Discussion

The present study showed that factors associated with life-space in older adults with aMCI were different from those reported by previous studies investigating older adults without cognitive impairment. The FoF, DSC and IADL maintained a significant association with the LSA scores in the stepwise multiple regression, whereas the TUG and sex did not have a significant association with life-space, unlike in the case of univariate analysis. It is possible that the restrictions of life-space for the aMCI participants were more affected by FoF, slower processing speed and restricted IADL than sex or physical performance.

FOF contributed to multiple aspects (e.g. physical function, cognitive function or psychological status)[30] and led to an unnecessary avoidance of activities for older adults, even though they might have been able to carry out these activities.[31,32] The present findings suggest that the association between FOF and activity restriction might become evident after life-space restriction in older adults with aMCI. Older adults with aMCI might potentially restrict activity accompanied by marginal IADL limitation. It is considered important to reduce FoF by targeting downstream factors, such as increasing physical functioning,[33] or improving medication use[34] and extending life-space activities for older adults with aMCI.

Life-space is a mobility indicator strongly related to cognitive function, particularly processing speed.[15] DSC is the primary measure of mental processing speed, clerical efficiency and visual-motor coordination.[35] The results of the present study suggest that processing speed is one of the factors related to life-space mobility in older adults and specifically suggests that processing speed might perform a more important role for maintaining life-space than other cognitive factors among aMCI individuals. Processing speed is an important domain of cognitive ability and might be useful as a biological marker of cognitive ageing.[36] For example, in terms of the important aspects of life-space, improving processing speed was closely associated with protection against declines in driving mobility[37] and delays in driving cessation[38] in older adults. Driving mobility is more likely to deteriorate in older adults with aMCI than those with healthy cognitive abilities.[9] It is possible that processing speed might be one of several important factors in maintaining not only driving mobility, but also life-space in the older adults, especially in those with aMCI. Furthermore, the assessment of processing speed might have implications for the prediction of decline in the life-space of older adults with aMCI.

A constricted life space is associated with increased risk of AD and cognitive decline among older persons.[39] Findings of the present study might contribute to development of interventions to expand life-space of older adults with aMCI. Specific approaches might be required for older adults with aMCI in order to maintain or expand life-space, such as multicomponent cognitive behavioural group intervention to reduce FoF and associated activity avoidance,[40,41] and speed of processing training.[37,38]

There were several limitations in the present study that need to be mentioned. First, the analyses were based on a cross-sectional design and we were therefore only able to examine the correlates of life-space. Second, the sample size was relatively small. To truly determine the decision factors shaping life-space among aMCI individuals, it is important to compare results between an equal number of participants with and without aMCI. Third, we did not collect data on certain factors that might influence the size of one's life-space, such as sensory function, acute illness or financial strain. These and other factors should be examined in future life-space studies. Finally, we did not compare associated factors in cases of normal older adults, older adults with AD, and older adults with multidomain MCI. Comparative studies on determinants of life-space covering the continuum from normal cognition through MCI to AD should be carried out in the future. Contribution of cognitive factors to life-space might increase with progression of cognitive impairment.

In summary, despite some limitations, this is the first study to explore the determinants of life-space in older adults with aMCI. The presence of FoF, slower processing speed and restricted IADL were more closely related to life-space than physical performance and demographic factors in older adults with aMCI. These findings give new insight into developing effective interventions for preventing life-space restrictions in cognitively frail older adults.

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ORIGINAL ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

# Characteristics of cognitive function in early and late stages of amnestic mild cognitive impairment

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**Aim:** The detection of the early stages in amnesic mild cognitive impairment (aMCI) is considered important in diagnosing progression to Alzheimer's disease. The current study sought to investigate differences in cognitive function between control subjects with no memory loss (control), and subjects in the early stage of aMCI (EMCI) and late stage of aMCI (LMCI).

**Methods:** A total of 100 community-dwelling older adults aged 65 years and over were recruited from 1543 potential subjects. Subjects were classified into three groups based on the degree of objective memory impairment; control ($n = 29$), EMCI ($n = 34$) and LMCI ($n = 37$). Multiple neuropsychological tests were carried out to examine cognitive function.

**Results:** The EMCI individuals showed lower cognitive function relative to controls; not only in logical memory, but also in letter fluency ($P < 0.05$). There were no significant differences in neuropsychological scores between the EMCI and LMCI groups, except for category fluency and logical memory. In addition, the EMCI subjects' logical memory score showed a significant relationship with letter fluency, category fluency and digit span backward test performance ($P < 0.05$).

**Conclusions:** These results suggest that the application of multiple neuropsychological tests might be useful in diagnosing older adults with EMCI and LMCI. **Geriatr Gerontol Int 2013; 13: 83–89.**

**Keywords:** cognitive function, dementia, executive function, memory, mild cognitive impairment.

## Introduction

Mild cognitive impairment (MCI) is a prodromal condition of Alzheimer's disease (AD). It is a reversible state that can improve or progress to AD. Indeed, amnestic MCI (aMCI) has a particularly high risk of progression to AD compared with normal aging.[1–3] MCI has become increasingly well understood in the past decade, although some studies have produced inconsistent results.[4] This variation in results might a result of the heterogeneity of MCI, particularly of aMCI.[4–6] To detect the earlier stages of aMCI, the severity of clinical impairment and pathology of this condition need to be clarified. To characterize an extended range of MCI to broaden the understanding of the early stages of AD, conventional stages of aMCI are considered to represent a late stage of aMCI (LMCI), and the gap between cognitively normal and LMCI is considered to represent the early stage of aMCI (EMCI).[7]

Memory deterioration is the core characteristic of both MCI and AD, and is strongly related to pathology in the medial temporal lobe (MTL).[6,8,9] Although the volume in the MTL can show decreases according to the spectrum of AD, predicting conversion to AD, the functional changes in the brain are thought to proceed non-linearly. MCI patients with some atrophy have been reported to show hyperactivation in the MTL compared with normal controls during a memory task, whereas MCI patients whose conditions were closer to AD showed hypoactivation similar to that found in AD

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patients.[5,6] These abnormal activations were found to correspond with the severity of memory decline in MCI, and compensation in the brain network might affect the severity of cognitive decline in MCI. However, the characteristics of cognitive function in the earlier stages of MCI, such as EMCI, have not been clarified.

Etiological data have confirmed not only a functional decline of memory in aMCI, but also other cognitive functional decline; for example, executive dysfunction in aMCI has been described as a risk factor for conversion to AD.[10–12] The declines of memory and other cognitive functions in MCI might reflect the abnormal activity of multiple domains in the brain. Memory is not only dependent on the pathology in MTL, but also on the connectivity of the MTL with the cingulate gyrus, frontal lobe and prefrontal lobe.[13–16] The loss of this connectivity in this neural network is linked to decreased cognitive function in aMCI.[13,17] Furthermore, in addition to the contribution of the MTL regions, decreased thickness in the prefrontal cortex and the posterior cingulate cortex has strong associations with lower memory and executive function in aMCI,[18] and lower executive function interfaces with memory performance in aMCI.[19] However, the characteristics of cognitive function, including executive function in EMCI, and the relationships between memory loss and other cognitive dysfunctions in EMCI remain unclear.

In the current preliminary study, we sought to compare cognitive function between EMCI and LMCI subjects. In addition, we wanted to determine the association between memory and other cognitive functions in elderly adults with EMCI or LMCI. Multiple neuropsychological tests measuring attention, verbal fluency, visual memory and logical memory were used to examine cognitive function.

## Materials and methods

### *Participants*

Participants were recruited from two volunteer databases ($n = 1543$), which included elderly adults aged 65 years and over who were selected by random sampling or who attended a health check carried out at a health center in Obu in 2009. The strata used for the stratified random sampling were age and sex. In the first eligibility assessment for the present study, 528 potential participants with a Clinical Dementia Rating of 0.5, or reporting memory complaints, were enrolled. A total of 165 participants responded to the second eligibility assessment, whereas 100 completed the assessment and met the inclusion criteria. To meet the inclusion criteria, participants had to be living independently in the community, be Japanese-speaking, possess adequate hearing and visual acuity, and be able to participate in the examinations. Additionally, general cognitive function was found to be intact in participants who had Mini-Mental State Examination (MMSE) scores between 24 and 30.[20] The exclusion criteria were: a history of major psychiatric illness, other serious neurological or musculoskeletal diagnoses and depression (Geriatric Depression Scale [GDS] score $\geq 10$[21]). The core concepts of aMCI in the present study were according to the Peterson's internationally accepted criteria:[22] having memory complaints and objective memory impairment, being independent in activities of daily living, preserved general cognitive function, and no dementia. The definition of objective memory impairment varies among previous reports. In the current study, we defined objective memory impairment using memory scores in the Wechsler Memory Scale-Revised (WMS-R) Logical Memory II,[23] based on the criteria of the Alzheimer's Disease Neuroimaging Initiative Grand Opportunity protocol.[24] In addition, we used cut-off scores in a modification of the category of educational history suited to the Japanese educational system to divide the aMCI stages as follows: EMCI (between 0.5 and 1.5 SD below the mean of normative data adjusting for educational history) and LMCI (more than 1.5 SD below the mean of normative data adjusting for educational history). Participants were classified into three groups; control subjects without significant objective cognitive impairments (control: $n = 29$); EMCI: $n = 34$; and LMCI: $n = 37$. The present study was approved by the ethics committee of the National Center for Geriatrics and Gerontology. All participants provided written informed consent.

### *Measurements*

Demographic data were recorded, including age, sex and educational history. All neuropsychological tests were carried out by well-trained speech therapists, and each score was rechecked by a single therapist who was blinded to the other data of the participants in the present study. General cognitive function was evaluated using MMSE.[20] The WMS-R Logical Memory II was carried out to examine logical memory. Visual memory was assessed using the Rey–Osterrieth Complex Figure Test (RCFT; 3 min and 30 min delay).[25,26] At the beginning of the test, participants were provided with a complex figure for the first time. Then, after 3 min and 30 min, these participants were asked to recall and draw, as accurately as possible, the original figure. Verbal fluency is composed of letter fluency and category fluency.[27] Participants were asked to generate as many words as possible within 1 min consisting of an initial letter (letter fluency) and an animal name (category fluency).[28] The verbal fluency test provides an evaluation of expressive language

**Table 1** Comparison of neuropsychological tests between groups

| Variables | Control ($n = 29$) | MCI EMCI ($n = 34$) | LMCI ($n = 37$) | $F$ | $P$-value |
|---|---|---|---|---|---|
| Mini-Mental State Examination (score) | 27.6 (2.0) | 26.6 (1.9) | 27.0 (1.9) | 2.28 | 0.107 |
| WMS-R Logical Memory II (score) | 10.8 (2.4) | 5.5 (1.6)† | 1.2 (1.3)†‡ | 230.7 | <0.0001 |
| RCFT 3 min (score) | 18.6 (5.6) | 15.0 (6.0)† | 14.0 (5.5)† | 5.57 | 0.005 |
| RCFT 30 min (score) | 17.6 (5.5) | 15.1 (5.8) | 13.0 (6.5)† | 4.81 | 0.01 |
| DS forward (score) | 8.3 (2.3) | 7.8 (2.2) | 7.4 (2.4) | 1.28 | 0.283 |
| DS backward (score) | 5.9 (1.6) | 5.4 (1.6) | 4.6 (1.6)† | 4.82 | 0.01 |
| Letter fluency (numbers) | 6.9 (3.1) | 5.2 (2.0)† | 5.3 (1.6)† | 5.13 | 0.008 |
| Category fluency (numbers) | 16.6 (5.0) | 15.8 (4.9) | 12.9 (3.5)†‡ | 6.49 | 0.002 |

†Compared with normal for post-hoc analyses at $P < 0.05$. ‡Compared between EMCI and LMCI for post-hoc analyses at $P < 0.05$. Values are means (SD) or proportion. Group differences were tested in all data using ANOVA. The statistical data are presented as $F$ and $P$-value. Control, control subjects without objective memory impairments; DS, digit span; EMCI, the early stage in amnesic mild cognitive impairment; LMCI, the late stage in amnesic mild cognitive impairment; MCI, mild cognitive impairment; RCFT, Rey–Osterrieth complex figure test; WMS-R, Wechsler Memory Scale-Revised.

ability and executive function.[25,27,28] We carried out a digit span forward test (DSF) and a digit span backward test (DSB). Both tests are subsets of the Wechsler Adult Intelligence Scale III, and require participants to repeat a series of verbally-presented digits of increasing length in forward and backward order.[25] Performance on the digit span task strongly depends on working memory, cognitive regulation and manipulation, all of which are components of executive function.

### *Statistical analyses*

Analyses of variance (ANOVA) or $\chi^2$-tests (for sex) were carried out to determine the differences in demographic data between the control, EMCI and LMCI groups. The comparison of each neuropsychological test between groups was analyzed using ANOVA and Tukey–Kramer honestly significant difference post-hoc tests. In addition, logistic regression analysis was carried out to identify the relationship between neuropsychological tests and cognitive impairment status. Crude odds ratios were calculated for each test (model 1) and logistic regression analysis was carried out, adjusted for age and sex (model 2). To examine the association between verbal memory and other neuropsychological tests, Pearson's correlation coefficients were calculated. We also used linear regression to assess the relationships between neuropsychological variables while controlling for age and sex. Statistical significance was set at $P < 0.05$. All analyses were carried out using commercially available software (JMP8.0J, SAS Institute Japan, Tokyo, Japan) for Windows.

## Results

Demographic characteristics (control: age = 72.8 ± 4.7, proportion of women = 62%, educational history = 10.3 ± 2.3; EMCI: age = 75.4 ± 7.2, proportion of women = 56%, educational history = 10.4 ± 2.1; LMCI: age = 76.8 ± 7.5, proportion of women = 41%, educational history = 11.3 ± 2.9) were not different between groups (age: $F = 2.62$, $P = 0.08$; sex: $\chi^2 = 3.35$, $P = 0.19$; educational history: $F = 1.69$, $P = 0.19$). The results of the neuropsychological measures are presented in Table 1. MMSE scores did not differ between groups. Group effects were observed in the RCFT (3 min: $P < 0.01$, 30 min: $P = 0.01$), DSB ($P = 0.01$), letter fluency ($P < 0.01$) and category fluency ($P < 0.01$). Both EMCI and LMCI showed lower function of letter fluency ($P = 0.01$) and WMS than the control ($P < 0.01$). DSB significantly decreased in LMCI compared with the control ($P = 0.01$), but not between other groups. DSF was not significantly different between groups. Scores in the neuropsychological tests, other than category fluency ($P = 0.02$) and logical memory ($P < 0.01$), did not differ between EMCI and LMCI. Table 2 shows the results of logistic regression analysis of the neuropsychological test results, discriminating EMCI subjects from control or LMCI subjects. In the control and EMCI groups, the RCF 3 min (model 1: $P = 0.02$, model 2: $P = 0.04$) and letter fluency (model 1: $P = 0.03$, model 2: $P = 0.04$) showed significant associations, whereas only category fluency (model 1: $P < 0.01$, model 2: $P < 0.01$) showed a significant difference between the EMCI and LMCI groups.

Table 3 shows the relationships of WMS-R Logical Memory II test with the neuropsychological tests. Over all participants, the WMS-R Logical Memory II test was significantly associated with RCFT 3 min, RCFT 30 min, DSB, letter fluency and category fluency scores, even after controlling for age and sex. In the EMCI group, DSB, letter fluency and category fluency were significantly related to WMS-R Logical Memory II test scores. However, there were no significant relationships

**Table 2** The results of logistic regression in neuropsychological tests for discriminating early stage in amnesic mild cognitive impairment subjects from control or late stage in amnesic mild cognitive impairment subjects

| Variables | Control and EMCI ($n = 63$) Odds ratio (95% CI) | | EMCI and LMCI ($n = 71$) Odds ratio (95% CI) | |
|---|---|---|---|---|
| | Model 1 | Model 2 | Model 1 | Model 2 |
| RCFT 3 min | 0.90 (0.82–0.99)* | 0.91 (0.83–0.99)* | 0.97 (0.89–1.05) | 0.97 (0.89–1.06) |
| RCFT 30 min | 0.92 (0.84–1.01) | 0.94 (0.85–1.03) | 0.94 (0.87–1.02) | 0.94 (0.87–1.02) |
| DS forward | 0.89 (0.71–1.12) | 0.89 (0.70–1.12) | 0.93 (0.76–1.15) | 0.92 (0.74–1.15) |
| DS backward | 0.82 (0.60–1.14) | 0.87 (0.62–1.22) | 0.75 (0.55–1.02) | 0.74 (0.54–1.03) |
| Letter fluency | 0.91 (0.83–0.99)* | 0.91 (0.83–0.99)* | 1.00 (0.92–1.09) | 0.99 (0.91–1.09) |
| Category fluency | 0.97 (0.88–1.07) | 0.99 (0.89–1.10) | 0.84 (0.74–0.96)** | 0.82 (0.71–0.94)** |

*$P < 0.05$; **$P < 0.01$. Model 1 is a crude model and model 2 was conducted adjusting for age and sex. CI, confidential interval; Control, control subjects without objective memory impairments; DS, digit span; EMCI, the early stage in amnesic mild cognitive impairment; LMCI, the late stage in amnesic mild cognitive impairment; RCFT, Rey–Osterrieth complex figure test.

**Table 3** Relationships between the Wechsler Memory Scale-Revised Logical Memory II test and neuropsychological tests

| Variables | Total | | EMCI | | LMCI | |
|---|---|---|---|---|---|---|
| | *r* | β | *r* | β | *r* | β |
| RCF 3 min | 0.36** | 0.30** | 0.04 | −0.0002 | 0.11 | 0.21 |
| RCF 30 min | 0.33** | 0.26** | 0.05 | −0.01 | 0.03 | 0.10 |
| DS forward | 0.13 | 0.08 | 0.28 | 0.16 | −0.09 | −0.07 |
| DS backward | 0.35** | 0.29** | 0.64** | 0.59** | −0.20 | −0.18 |
| Letter fluency | 0.32** | 0.28** | 0.48** | 0.39* | −0.19 | −0.22 |
| Category fluency | 0.39** | 0.35** | 0.43* | 0.35* | 0.20 | 0.16 |

*$P < 0.05$; **$P < 0.01$. Pearson *r*-values represent the simple correlation between the Wechsler Memory Scale-Revised Logical Memory II test and the dependent variables. A standardized beta (β) represents the correlation between logical memory and each dependent variable after controlling for age and sex. Control, control subjects without objective memory impairments; DS, digit span; EMCI, the early stage in amnesic mild cognitive impairment; LMCI, the late stage in amnesic mild cognitive impairment; RCFT, Rey–Osterrieth complex figure test.

between the WMS-R Logical Memory II test and the other neuropsychological measurements in the LMCI group.

## Discussion

The present preliminary study shows the characteristics of cognitive function in EMCI and LMCI participants. We classified the participants into three groups by the stage of aMCI, showing group differences in cognitive decline. Significantly lower neuropsychological performance scores in RCFT, DSB, letter fluency and category fluency were found in the LMCI group compared with control participants. The EMCI group also showed significantly lower cognitive performance in the letter fluency and RCFT compared with the control group, whereas significant differences in cognitive function between the EMCI and LMCI groups were only found in the category fluency and in the WMS-R Logical Memory II test. These group differences remained after adjusting for age and sex. These findings suggest that this method is useful in distinguishing EMCI from other groups. The correlational analysis further examined the characteristics of EMCI. A significant relationship between WMS-R Logical Memory II test with verbal fluency and DSB was confirmed in the EMCI participants, but not LMCI participants, after adjusting for age and sex.

Decline in cognitive function was mainly observed in memory, and other cognitive functions also deteriorated in elderly participants with MCI. The present results in LMCI participants are consistent with other studies in which aMCI subjects showed lower performance in the RCFT,[29] DSB[30] and verbal fluency test[30–33] compared with control subjects. The decline of RCFT and letter fluency performance also occurred in EMCI individuals in the present study. RCFT performance reflects the