Table 1 Characteristics, reaction times, and neurocognitive functions in the participants in the non-amnestic mild cognitive impairment and amnestic mild cognitive impairment groups

Characteristics	non-aMCI ($n = 62$)	aMCI ($n = 36$)	P-value
Age (years)	74.0 (6.1)	76.2 (7.2)	0.119
Sex, n (%)			
Male	26 (41.6)	21 (58.3)	0.117
Female	36 (58.1)	15 (41.7)	
Diagnosis, n (%)			
Hypertension[†]	31 (50.8)	13 (36.1)	0.160
Diabetes mellitus	6 (9.7)	5 (13.9)	0.524
Medication[†] (three or more)	22 (36.1)	17 (50.0)	0.186
GDS (score)	3.0 (2.3)	2.9 (2.4)	0.857
Reaction time/dual-task performance			
Simple reaction time (ms)	257.6 (45.9)	260.8 (41.7)	0.734
Dual-task reaction time (ms)	398.5 (117.2)	473.5 (171.2)	0.012
General cognitive function			
MMSE (score)	27.0 (2.0)	27.1 (1.8)	0.858
Visual memory			
ROCF[‡] (score)	16.4 (5.7)	12.8 (6.5)	0.008
Working memory			
Digit Span Forward–Backward (score)	2.5 (2.3)	2.8 (1.9)	0.458
Executive function			
Trail Making Test Part B–Part A[‡] (s)	52.8 (86.4)	73.6 (75.5)	0.245
Processing speed			
Digit Symbol-Coding (score)	47.6 (15.7)	47.3 (15.2)	0.934

The data are expressed as the mean (SD) score unless otherwise indicated. Significance was arbitrated at $P < 0.05$ using the unpaired Student's t-test or χ^2-test (for sex and diagnosis). [†]One participant in the non-amnestic mild cognitive impairment (aMCI) group did not report whether he or she had hypertension. One participant in the non-aMCI group and two participants in the aMCI group could not describe their current medication. [‡]One participant in the aMCI group did not complete the Rey-Osterrieth Complex Figure Test (ROCF). Two participants in the aMCI group and two participants in the non-aMCI group did not complete the Trail Making Tests. GDS, Geriatric Depression Scale; MMSE, Mini-Mental State Examination.

analysis to examine dual-task RT, we found a R^2-value of 30.5% and a standardized β-value of 0.298 for executive function assessed by the delta TMT ($P = 0.006$).

Discussion

The present results examined the relationships between neurocognitive measures and dual-task performance (measured by RT to visual stimuli) in older adults with MCI. The aMCI participants showed specific deficits in dual-task performance compared with the non-aMCI participants, and low dual-task performance was associated with declines in executive function in older adults with MCI.

A large number of previous studies reported a relationship between dual-task performance and cognitive function, particularly attentional capacity[28] and executive function.[29–32] Executive function plays an important role in older adults' ability to effectively adapt to complex environments and to adequately allocate the attentional resources necessary for successfully completing a given task.[28,29,33,34] Additionally, executive function is an important mediator of memory function in older adults suffering from age-related functional decline,[35] and MCI.[36] In the present study, we found that increased attentional costs under dual-task conditions were related to reduced executive function in older people with MCI. These findings are in accord with the results of previous studies showing a relationship between dual-task costs and neurocognitive functions. However, the relationship between the Digit Symbol-Coding scores, the delta TMT and dual-task RT in the aMCI group did not remain after controlling for age and education. Our data could not provide a definite association between dual-task performance and neurocognitive functions in the aMCI participants.

Dual-task performance reflects divided attention and is considered an important executive function.[3,4] Therefore, it would be expected that participants with non-aMCI showed lower dual-task performance based on

Table 2 Bivariate correlations between reaction times and neurocognitive functions

Outcome measure	Non-aMCI (n = 62)				aMCI (n = 36)			
	Simple-task RT		Dual-task RT		Simple-task RT		Dual-task RT	
	Simple-Correlation (r)	Age and education-controlled (β)	Simple-correlation (r)	Age and education-controlled (β)	Simple-correlation (r)	Age and education-controlled (β)	Simple-correlation (r)	Age and education-controlled (β)
MMSE	−0.089	0.006	−0.102	−0.035	−0.221	−0.177	−0.231	−0.083
ROCF	−0.084	0.004	−0.317*	−0.275*	−0.081	−0.038	−0.180	0.027
Digit Span Forward–Backward	−0.175	−0.215	−1.000	−0.130	−0.218	−0.191	−0.066	0.105
Trail Making Test Part B–Part A	0.251	0.171	0.429**	0.380**	0.025	0.043	0.370*	0.229
Digit Symbol-Coding	−0.282*	−0.111	−0.386**	−0.363*	−0.135	−0.042	−0.402*	−0.163

*$P < 0.05$, **$P < 0.01$. aMCI, amnestic mild cognitive impairment; MMSE, Mini-Mental State Examination; ROCF, Rey-Osterrieth Complex Figure Test; RT, reaction time.

criteria for classification of groups. Contrary to expectations, the aMCI group showed significantly lower dual-task performance than the non-aMCI group in the present study. The aMCI group included not only participants with amnestic single domain MCI subtype (showing a memory deficit), but also those with amnestic multiple domain MCI subtype (showing deficits of memory in addition to other domains). The results of the present study showed that there were no statistically significant between-group differences in other domains, such as executive function and processing speed. The present findings might suggest that older adults showing deficits of multiple domains including memory deficits exhibit decline of dual-task performance compared with those without memory deficits. Unfortunately, it was difficult to analyze using detailed subtype categories of MCI, because the sample size was small. Clarifying these problems by future research with a large sample size would be required.

The present findings indirectly corroborate a number of other studies, showing that patients with MCI experienced high dual-task costs.[11,37,38] Previous studies reported that dual-task-related changes in performance were greater in patients with MCI compared with cognitively normal age-matched controls,[37,38] and that dual-task performance during walking was significantly impaired in MCI patients.[11] However, the current findings conflict with the results of some previous studies. One study reported that there were no differences in dual-task performance between aMCI patients and controls.[14] Additionally, in a study using the Talking While Walking assessment as a dual-task test, no differences in dual-task performance were reported between MCI and healthy participants, although participants with AD showed greater performance changes between single task and dual-task conditions compared with healthy participants.[39] Previous results regarding the relationships between cognitive status and dual-task decrements among older adults at risk of dementia have not been consistent, particularly for MCI patients.[6,7,40] Studies investigating the relationship between dual-task performance and cognitive status have tended to focus on patients with AD, who generally show impaired dual-task performance. AD patients also show difficulties in dual-task performance requiring the completion of a cognitive task while walking.[7,40] These results suggest that the ability to divide attention, in combination with a cognitive task, is reduced among patients with AD. Thus, decreased dual-task performance might be considered an early symptom of AD. Although the present study included only MCI patients, our findings provide indirect evidence that poor dual-task performance with cognitive demand might be related to impaired executive functioning in older adults with MCI.

Executive functions are higher order cognitive processes that control, integrate, organize and maintain

Table 3 Multiple linear regression model summary for simple reaction time and dual-task reaction time experiments

Independent Variable	Simple reaction time (ms)			Dual-task reaction time (ms)		
	R^2	Standardized β	*P*-value	R^2	Standardized β	*P*-value
Model	0.130			0.305		
Group (aMCI)		0.028	0.797		0.184	0.061
Age		0.153	0.233		0.211	0.067
Education		–0.155	0.175		–0.073	0.470
MMSE		–0.059	0.213		0.052	0.622
ROCF		0.051	0.661		–0.107	0.302
Digit Span Forward–Backward		–0.216	0.038		–0.071	0.433
Trail Making Test Part B–Part A		0.137	0.246		0.298	0.006
Digit Symbol-Coding		0.030	0.829		–0.063	0.616

Dependent variable: simple reaction time (ms) and dual-task reaction time (ms). aMCI, amnestic mild cognitive impairment; MMSE, Mini Mental State Examination; ROCF, Rey-Osterrieth Complex Figure Test.

other cognitive abilities.[41] Associations between physical performance and executive function were shown in community-dwelling older adults.[42] Similarly, these associations were confirmed in older adults with MCI.[43] The beneficial effects of physical exercise have been shown in older adults with MCI.[44,45] It might be clinically important to improve executive function among older adults with MCI, because deficits in executive function strongly predict conversion to AD.[46] The results of the present study support the hypothesis that interventions that include the dual-task paradigm might be effective for increasing executive function among older adults with MCI.

Several limitations of the current study should be considered. First, we used cross-sectional data, meaning causal relationships could not be assessed. For lack of longitudinal cognitive changes, the results of the present study fail to indicate that measurements of dual-task performance might be useful as a prognostic measure of cognitive decline. Second, the absence of a large sample size limits the conclusions that can be drawn. The sample size of aMCI participants was markedly smaller than the non-aMCI participants, limiting the interpretation of the results. Third, we could not assess whether the participants correctly and rapidly participated in the concurrent task (counting backwards) that relied on increasing demands of the dual-task. In the present study, it was important for the participants to divide their attention during the dual-task conditions. Although participants in both groups showed significantly longer RT under the dual-task conditions compared with the simple-task conditions, some participants would divide the minimum attention required to complete the concurrent tasks. Finally, our study cohort did not contain healthy subjects or AD patients, meaning that we could not examine the association between dual-task performance and the risk of cognitive decline in AD-related processes. In addition, analysis of neuroimaging data was not included in the present study. MCI represents a complex heterogenous condition, including degenerative and vascular brain pathologies. Brain conditions potentially affect cognitive decline including dual-task performance.[47]

In conclusion, we found that aMCI patients showed deficits in dual-task performance compared with non-aMCI participants, and poor dual-task performance was associated with declines in executive function in older people with MCI. Future longitudinal and interventional studies should investigate the use of dual-task testing with varying levels of cognitive demand in subjects at risk of dementia, and analyses of imaging data, because these studies might elucidate the factors that lead to the conversion to AD from MCI.

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Disclosure statement

There are no financial and personal relationships with other people or organizations that may lead to a conflict of interest.

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Aging Clinical and Experimental Research

The relationship between atrophy of the medial temporal area and daily activities in older adults with mild cognitive impairment

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ABSTRACT. ***Background and aims:*** *Many studies have suggested that social network, leisure activity, and physical activity can have protective effects against dementia and Alzheimer's disease. However, previous studies have not examined the relationship between daily activities and brain atrophy in older adults. This study aimed to explore what kind of daily activities were associated with atrophy of the medial temporal area including the entorhinal cortex (MTA-ERC) in older adults.* ***Methods:*** *In total, 122 older adults (aged 65 and over) with subjective memory complaints or a Clinical Dementia Rating of 0.5 underwent magnetic resonance imaging, and MTA-ERC atrophy was assessed by the voxel-based morphometry method. Based on magnetic resonance imaging data, the subjects were divided into atrophy and non-atrophy groups. Daily activities were assessed using a 20-item questionnaire (e.g., instrumental activities of daily living, social activities), and we compared activity participation between the groups.* ***Results:*** *The atrophy group (n=37) showed significantly lower participation in 4 out of 20 activity items (cleaning, intellectual activity, culture lessons, and using a personal computer) than the non-atrophy group (n=85). Summed scores of these 4 items (range from 0 to 4) were significantly associated with MTA-ERC atrophy even after adjustment for age, sex, education status, and Mini-Mental State Examination score.* ***Conclusions:*** *In conclusion, MTA-ERC atrophy was associated with cognitive activities or household-related activities requiring planning.*
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INTRODUCTION

Memory impairment is the earliest symptom of Alzheimer's disease (AD) in most patients (1), and brain atrophy of the medial temporal region is observed in those patients (2). The medial temporal lobe has long been known to play a critical role in memory (3). In a recent review, the most reliable and well-documented finding was an association between impaired verbal memory and medial temporal lobe atrophy that is particularly robust for the hippocampal and entorhinal regions (3). Moreover, hippocampal and entorhinal cortex atrophy have been shown to predict conversion to AD (1, 4, 5). It is important to assess atrophy of the medial temporal areas (MTA), especially the hippocampus and entorhinal cortex for understanding AD pathology.

Many studies have suggested that social network, leisure activity, and physical activity have protective effects against dementia and AD (6-13). For example, a popu-

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Key words: Alzheimer's disease, magnetic resonance imaging, brain atrophy, activities of daily living.

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lation-based longitudinal study, with a mean follow-up of 6.2 years, confirmed a reduced incidence rate of dementia for people who exercised 3 or more times a week (13.0 per 1000 person-years), compared with those who exercised fewer than 3 times per week (19.7 per 1000 person-years). People who exercised 3 or more times a week had a relative hazard of 0.68 (CI 0.48-0.96) for developing dementia compared with those who exercised fewer than 3 times per week (12). Moreover, Scarmeas et al. (7) demonstrated that engagement in leisure activities may reduce the risk of incident dementia. These findings support the hypothesis that physical and leisure activities reduce the likelihood for cognitive decline in community-dwelling older adults.

Some studies have failed to observe the benefits of physical activity (or exercise) in preserving cognitive function (14-18), suggesting that the effects of physical activity on cognitive functions might change according to the type of activity; but most of the studies examined the effects of composite physical activity (17), and the effect of individual activities is not well known. Furthermore, these previous studies did not examine brain atrophy; the relationship between these activities and brain atrophy (especially the MTA) was not clear.

To address these issues, we recruited community-dwelling older adults who had memory problems and conducted magnetic resonance imaging (MRI). The purpose of this study was to determine what kind of daily activity was associated with MTA atrophy as assessed by the voxel-based morphometry method.

METHODS

Subjects

The subjects were recruited from two volunteer databases (n=1543) that included elderly (aged 65 and over), who were selected by random sampling or who attended a health check in Obu, Japan. In the first eligibility assessment of this study, 528 potential subjects who had a Clinical Dementia Rating of 0.5 or memory complaints were enrolled. One hundred sixty-five subjects responded to the second eligibility assessment, and 125 out of 165 subjects completed all assessments. People who needed assistance for basic activities of daily living or who had neurological or psychiatric illness, cardiovascular disease, head trauma, drug abuse issues, alcoholism, severe pain, and contraindication of MRI were excluded. Finally, 122 subjects remained and met the definition of MCI using Petersen criteria (19).

All subjects received an MRI, a questionnaire on daily activity, and neuropsychological tests; Mini-mental State Examination (20) and Wechsler Memory Scale-Revised (WMS-R) Logical Memory (21) were assessed by speech therapists. Depressive symptoms were assessed by the Geriatric Depression Scale (22). The details of the study were explained to all subjects in advance, and written consent was obtained from each subject. In addition, this study was conducted in accordance with the Helsinki Declaration, and was approved by the ethics committee of the National Center for Geriatrics and Gerontology.

MRI procedure and voxel-based MRI analysis

We determined the atrophy of MTA including the entorhinal cortex (MTA-ERC) using the voxel-based specific regional analysis for Alzheimer's disease (VSRAD) (23-25), which yields a Z-score as the end point for the assessment of medial temporal lobe volume. MRI was performed using a 1.5-T system (Magnetom Avanto, Siemens, Germany). Three-dimensional volumetric acquisition of a T1-weighted gradient echo sequence was then used to produce a gapless series of thin sagittal sections using a magnetization preparation rapid-acquisition gradient-echo sequence (repetition time, 1700 ms; echo time, 4.0 ms; flip angle 15°, acquisition matrix 256 × 256, 1.3-mm slice thickness). According to the VSRAD procedure proposed by Matsuda and Hirata et al. (23, 25), the acquired MRI images were reformatted to gapless 2-mm thin-slice transaxial images.

In the voxel-based MRI analyses, the first anatomical standardization used affine transformation. The normalized MRI images were then segmented into gray matter, white matter, cerebrospinal fluid and other components using a modified version of the clustering algorithm, the maximum likelihood "mixture model" algorithm. The segmentation procedure involved a calculation for each voxel using a Bayesian probability of belonging to each tissue class based on *a priori* MRI information with a nonuniformity correction. The segmented gray matter images were then subjected to an affine and non-linear anatomical standardization using an *a priori* gray matter template. The anatomically standardized gray matter images were smoothed with an isotropic Gaussian kernel 12 mm full-width at half-maximum to exploit the partial volume effects, so as to create a spectrum of gray matter intensities. Gray matter intensities are equivalent to the weighted average of gray matter voxels located in the volume fixed by the smoothing kernel. Each gray matter image of the patients was compared with the mean and SD of gray matter images of the healthy volunteers using voxel-by-voxel Z-score analysis after voxel normalization to global mean intensities: Z-score = (control mean-individual value) / (control SD). The Z score thus reflected the degree of atrophy in bilateral MTA-ERC. Higher Z scores indicate clearer MTA-ERC atrophy.

Daily activities assessment

Daily activities were assessed using a questionnaire of 20 items that originated from brainstorming. The members who participated in brainstorming were 4 male physical therapists (the years of experience as a physical therapist were 18 years, 9 years, 4 years, and 1 year, respectively) and 2 female office workers (a married woman and a single woman). They discussed and chose the questionnaire items based on what was necessary for older adults to live independently in the community. In the present study, we used the 20 activity items (e.g., instrumental activities of daily living, social activities) that remained after discussion. We excluded items for basic activities of daily living (such as taking a bath, going to the toilet, and changing clothes) from the present questionnaire because all of our subjects were living independently in a community. The details of the questionnaire can be found in the *Appendix*. The subjects were asked whether they did each activity during the past one month, and they answered "yes (did)" or "no (did not)".

Statistical analysis

Subjects were divided into two groups: older adults without or with slight atrophy (Z score <2; non-atrophy group) and those with moderate or severe atrophy (Z score ≥2; atrophy group) in the MTA-ERC based on the results of the VSRAD. At first, we conducted an unpaired t-test or chi-square test to compare the characteristics of the subjects and the proportions of each daily activity in the two groups. If there were significant differences in the proportions of daily activity, we assigned 0 (did not) or 1 point (did) to these items in accordance with subject's response. Then, we summed the number of points by each subject. Second, multiple logistic regression analysis was performed to examine the independent associations between MTA-ERC atrophy and daily activity adjusted for demographic variables. We used moderate or severe MTA-ERC atrophy (Z score ≥2) as the dependent variable. The independent variables included age, sex, education status, MMSE score, state of achievement of each daily activity, and the summed score of daily activities (0 to 4). Statistical analysis was done using SPSS 12.0 for Windows, and all statistics were processed at a significance level of $p<0.05$.

RESULTS

The characteristics of the atrophy group (Z score ≥2; n=37) and the non-atrophy group (Z score <2; n=85) are listed in Table 1. There were significant differences in age (74.3±6.9 *vs* 79.5±6.2, $p<0.01$), sex (men/women=35/50 *vs* 26/11, $p<0.01$), education (10.9±2.7 *vs* 9.5±2.0, $p<0.01$), and MMSE score (26.7±2.2 *vs* 25.4±3.1, $p<0.05$) between the two groups. However, there were no significant differences in other characteristics.

In regard to 4 activity items (cleaning, intellectual activity, culture lesson, using a personal computer), the atrophy group had a significantly lower proportion of the people who had answered "yes (did)" than the non-atrophy group ($p<0.05$). Other items did not show significant differences between groups (Table 2). Therefore, the summed score included the number of those activity items where group differences were found and ranged from 0 to 4. The mean values of the summed score of the atrophy and non-atrophy groups were 1.5±1.1 and 2.4±1.0, respectively.

In multiple logistic regression analysis, no association was observed between MTA-ERC atrophy and the proportions of each daily activity, whereas the summed score showed a significant relationship with MTA-ERC atrophy even after adjustment for age, sex, education, and MMSE (odds ratio 0.576, 95% CI 0.358-0.924, $p=0.022$; Table 3).

DISCUSSION

Atrophy of the medial temporal lobe, especially the hippocampus and entorhinal cortex, is an MRI-based measure validated to predict conversion and understand progression to AD (1, 4, 5). In recent studies, the VSRAD was used to automatically and quantitatively assess MTA-

Table 1 - *Characteristics of the subjects.*

Variables		Z score <2 (n=85)	Z score ≥2 (n=37)	p-value
Age	year	74.3±6.9	79.5±6.2	<0.001**
Men	n (%)	35 (58.8)	26 (29.7)	0.003**
Education	year	10.9±2.7	9.5±2.0	0.003**
MMSE	score	26.7±2.2	25.4±3.1	0.028*
GDS	score	3.6±3.2	4.1±2.9	0.477
Atrophy of MTA-ERC	z-score	0.9±0.5	2.7±0.7	<0.001**
Diagnosis				
CVD	n (%)	3 (3.5)	3 (8.1)	0.258
Hypertension	n (%)	28 (32.9)	17 (45.9)	0.171
Diabetes mellitus	n (%)	10 (11.8)	1 (2.7)	0.088

Values are mean±SD or n (%). **$p<0.01$; *$p<0.05$. MMSE: Mini-mental State Examination; GDS: Geriatric Depression Scale; MTA-ERC: Medial temporal area including the entorhinal cortex; CVD: Cerebrovascular disease.

Table 2 - *The relationship between atrophy of the medial temporal area and individual daily activities in atrophy and non-atrophy groups.*

No	Item		Z score <2		Z score ≥2		p-value
			(n=85)		(n=37)		
1	Reading	n (%)	83	(97.6)	36	(97.3)	0.665
2	Going to a neighborhood	n (%)	84	(98.8)	37	(100.0)	0.697
3	Cleaning	n (%)	83	(97.6)	29	(78.4)	0.001**
4	Talking by telephone	n (%)	82	(96.5)	33	(89.2)	0.124
5	Taking out garbage	n (%)	74	(87.1)	31	(83.8)	0.631
6	Talking with somebody	n (%)	80	(94.1)	35	(94.6)	0.641
7	Caring for a grandchild	n (%)	59	(69.4)	22	(59.5)	0.285
8	Gardening	n (%)	70	(82.4)	28	(75.7)	0.394
9	Going out by bus or train	n (%)	73	(85.9)	30	(81.1)	0.501
10	Sports or hobbies	n (%)	61	(71.8)	20	(54.1)	0.057
11	Intellectual activities	n (%)	54	(63.5)	15	(40.5)	0.019*
12	Attending a meeting	n (%)	44	(51.8)	22	(59.5)	0.433
13	Working as a coordinator	n (%)	28	(32.9)	7	(18.9)	0.115
14	Culture lessons	n (%)	45	(52.9)	9	(24.3)	0.003**
15	Going to unknown place	n (%)	46	(54.1)	16	(43.2)	0.269
16	Carrying a heavy load	n (%)	62	(72.9)	26	(70.3)	0.762
17	Managing money	n (%)	85	(100.0)	35	(94.6)	0.090
18	Visiting friends	n (%)	69	(81.2)	28	(75.7)	0.489
19	Operating a video	n (%)	33	(38.8)	9	(24.3)	0.111
20	Using a personal computer	n (%)	23	(27.1)	4	(10.8)	0.047*

Values are the number (%) answered "yes (did)". **$p<0.01$; *$p<0.05$.

ERC atrophy and has been introduced for the diagnosis of Alzheimer-type dementia with MRI. Hirata et al. (23) found a high accuracy (87.8%) for discriminating patients with very early AD at the mild cognitive impairment (MCI) stage from control subjects by VSRAD. It is assumed that VSRAD data are effective for assessing initial brain atrophy in an AD progression process. To determine the relationship between MTA-ERC atrophy and daily activities, we conducted MRI scanning and an interview on detailed daily activities in older adults who had memory problems, but not dementia.

In the group comparison, there were significant differences in age. A previous study found a correlation between increasing age and decreasing brain volume (26), and found that brain atrophy may accelerate with increasing age (27). Our results are consistent with previous studies, and suggest that MTA-ERC atrophy was affected by advancing age. On the other hand, there were no significant differences in vascular risk factors, such as hypertension, diabetes mellitus, and cerebrovascular disease. White-matter changes appear to be more frequent in individuals with vascular risk factor, and apathy is a prominent syndrome related to cerebral white-matter changes (28). We consider that this result reflects the equivalence of subcortical vascular damage in both groups.

Older adults who carried out cleaning activity, intellectual activity, a culture lesson, and personal computer

Table 3 - *Relationship between atrophy of the medial temporal area and daily activities.*

Variables		OR	95% CI	p-value
Cleaning	(yes/no)	0.143	(0.020-1.013)	0.052
Intellectual activities	(yes/no)	0.510	(0.204-1.279)	0.151
Culture lessons	(yes/no)	0.484	(0.174-1.343)	0.163
Using a personal computer	(yes/no)	0.407	(0.103-1.608)	0.200
Summed scores of activities	(0-4)	0.576	(0.358-0.924)	0.022*

Dependent variable, the presence of medial temporal area atrophy (Z score ≥2). *$p<0.05$ (adjustment for age, sex, education, MMSE score). OR: odds ratio; CI: confidence interval; MMSE: Mini-Mental State Examination.

use were significantly less likely to have moderate to severe MTA-ERC atrophy than the older adults who did not carry out those activities. These are activities that were cognitively stimulating or required planning rather than simply physical activity itself. The risk of dementia is reduced by daily activities, particularly leisure activities (e.g., reading, playing board games, playing musical instruments, and dancing) (17) or other activities (knitting, doing odd jobs, gardening, and traveling) (15). However, these daily activities have not been examined in association with brain atrophy, although the analysis of MTA-ERC atrophy may lead to an understanding of why older adults who maintained daily activities demonstrated a decreased risk for decline in cognitive function and dementia compared with inactive older adults. Moreover, there was one report that MCI patients were significantly impaired in 14 out of 18 activities, particularly memory activities such as finding things at home, keeping appointments, and remembering information from conversations or from the television, or complex reasoning activities, such as checking bank accounts, writing letters or notes, preparing meals, traveling, or shopping (29). MCI is the prodromal stage of AD, and memory decline and brain atrophy particularly in MTA were characterized in this stage. Our findings indicated that some daily activities involving cognitive stimulation or household-related planning were associated with MTA-ERC atrophy. Limitations on daily activities, such as cleaning, intellectual activity, culture lesson, and using a personal computer, may be characteristic of older adults with a higher rate of MTA atrophy. To discover the risk of AD early, it will be useful to assess the level of cognitively stimulating activities. However, cleaning activity can be further examined because our results indicated that the non-atrophy group contained significantly more women. This activity is usually considered to be female-associated work. Furthermore, education modifies the relationship of AD pathology to cognitive function (30), and the higher degree of education may lead to engagement in more complex activities (e.g., using a personal computer). The non-atrophy group had a higher education level compared with the atrophy group in our study. Thus, it is possible that group differences in activity level may be associated with sex or education.

In multiple logistic regression analysis adjusted for age, sex, education, and MMSE score, no statistically significant associations were observed between MTA-ERC atrophy and the proportion of execution of each daily activity, whereas the summed score of significant activity items was significantly associated with MTA-ERC atrophy. We assessed only whether subjects did or did not do each activity during the past one month. There is a possibility that the simple assessment of the activities was unable to reflect the true activity status of the subjects. It might be one reason we did not observe an association between MTA-ERC atrophy and individual activities. On the other hand, the summed score of daily activities may reflect activity status and was associated with MTA-ERC atrophy in the older adults. These results are almost consistent with a previous study that examined the association between the risk of AD and composite cognitive activity (16-18). Perhaps it will be difficult to inhibit brain atrophy only by specific activity. As for the association with MTA-ERC atrophy, composite cognitive activity is a stronger measure than a specific cognitive activity.

Environmental enrichment is known to profoundly affect the central nervous system at the functional, anatomical, and molecular levels, and during the critical period and adulthood, which was confirmed in an experimental study using animals (31). In other animal studies, there were several reports that learning caused synaptogenesis in cerebellar cortex (32) and exercise enhanced hippocampal neurogenesis in the hippocampus (33). In humans, one study reported that aerobic exercise training increased brain volume (34). These findings have suggested that physically or cognitively stimulating activities cause neurogenesis of the cerebral nerve and enhancement of the neural network, further supporting the findings in this study.

There were no significant associations between individual physical activities (such as sports, going out, and gardening) and MTA-ERC atrophy in the present study. We cannot conclude that physical activity and MTA-ERC atrophy were unrelated because it is difficult to extract only physical activities from the questionnaire, which addressed daily activities. Little is known about the relationship between brain volume and physical activity in older adults. Aerobic exercise training has been shown to increase brain volume (34), and the regions of increased brain volume were anterior cingulate cortex, supplementary motor cortex, right inferior frontal gyrus, left superior gyrus, and anterior white matter. In the present study, there was no relationship between MTA-ERC atrophy and a habit of sports activities. Although sports involve aerobic exercise, the type of sport varies in the level of endurance and movement required and overall length performed. Thus, the relationship between sports activities and MTA requires in-depth study for comprehensive examination. Further research is needed to identify what regions are associated with physical activities and what physical activity in daily life is associated with MTA-ERC atrophy in older adults.

There are several limitations in this study. First, because the relationship between MTA-ERC atrophy and daily activities was examined using a cross-sectional design, it was difficult to prove any causal relationship. Second, frequency and duration of participation was not assessed for each daily activity. The relationship between MTA-ERC atrophy and the frequency of participation in daily activities was not clear. Previous studies examining the association between physical or leisure activity and the risk of dementia showed the reduction in risk is related to the frequency of participation (12, 17). Therefore, daily activity must be assessed in detail. Third, our results showed significant differences in age, sex, and educational level between the atrophy and non-atrophy groups. These factors would have a strong influence on brain atrophy or daily activities. In particular, epidemiologic evidence suggests a correlation between increasing age and decreasing brain volume (26), and brain atrophy may accelerate with increasing age (27). Even though we adjusted age in multivariate analysis, we might not have completely removed the influence of age. Finally, we did not get the information on the other factors that affect lifestyle (e.g. family member, place of living, income, cultural difference). This information may be more useful to understand the association between brain atrophy and daily activities. Additional analysis adjusted for potential confounding factors would be required in the future.

CONCLUSIONS

In conclusion, the older adults who carried out cleaning, intellectual activity, a culture lesson, and personal computer use were a significantly lower proportion of the people who had moderate to severe MTA-ERC atrophy compared with the older adults who did not carry out these activities. The summed score of the daily activities was independently associated with MTA-ERC atrophy, suggesting that MTA-ERC atrophy is associated with cognitively stimulating activities or household-related activities requiring planning rather than physical activities in older adults. To determine the effect of intellectual activities on MTA-ERC volume, a longitudinal or an interventional study is necessary.

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APPENDIX 1: Daily activities assessment

Remember the past one month, and please answer whether you did or did not do the following activities. (Please check yes or no.)

		Yes	No
1	Did you read a book or a newspaper?		
2	Did you go to a neighborhood by yourself?		
3	Did you clean your house?		
4	Did you talk by telephone?		
5	Did you take out garbage?		
6	Did you talk with somebody every day?		
7	Did you take care of a grandchild or a pet?		
8	Did you work on a garden or farm?		
9	Did you go out by bus or train by yourself?		
10	Did you do some sports or hobbies?		
11	Did you do any intellectual activities (such as a game or learning)?		
12	Did you attend a community meeting?		
13	Did you work as a coordinator like a group leader?		
14	Did you take any culture lessons?		
15	Did you go to an unknown place with a map?		
16	Did you carry a heavy load when shopping?		
17	Did you manage money by yourself?		
18	Did you visit your friends?		
19	Did you operate a video or a DVD player?		
20	Did you use a personal computer?		

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Original Research Article

Effects of Exercise Intervention on Vascular Risk Factors in Older Adults with Mild Cognitive Impairment: A Randomized Controlled Trial

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Key Words
Cholesterol · Rehabilitation · Cognitive impairment · Metabolic profiles · Dementia · Vascular risk factors · Physical activity

Abstract

Aims: The purpose of this study is to clarify the effects of exercise intervention on vascular risk factors in older adults with mild cognitive impairment (MCI). ***Methods:*** Community-dwelling older adults who met the definition of MCI using the Petersen criteria ($n = 100$; mean age = 75.3 years) were randomly allocated to the exercise ($n = 50$) or education control group ($n = 50$). Participants in the exercise group exercised under the supervision of physiotherapists for 90 min/day, 2 days/week, 80 times for 12 months. Anthropometric profiles, blood markers, blood pressure, and physical fitness (the 6-min walking test) were measured. Total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and TC/HDL-C risk ratio measurements were taken from blood samples. ***Results:*** The exercise group showed significantly reduced TC and TC/HDL-C risk ratio after training compared with baseline levels ($p < 0.001$, $p = 0.004$). However, no significant reduction was found for the control group ($p = 0.09$, $p = 0.09$). Physical fitness also significantly improved after exercise intervention compared with the control group ($p < 0.0001$). ***Conclusion:*** Exercise intervention was associated with positive changes in important vascular risk factors related to cognitive decline and vascular disease in older adults with MCI.

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Introduction

Cognitive problems in older adults range from mild impairment to severe dementia. The transitional stage between normal aging and dementia has been designated as mild cognitive impairment (MCI) [1, 2]. Individuals with MCI have been found to have a 10–15 times higher risk of developing Alzheimer's disease (AD), although up to 40% will not develop dementia [3]. It is of great importance to recognize and treat patients at the earliest stage of the disease [4]. Recent studies have reported beneficial effects of physical activity or exercise on cognitive health, such as cognitive function [5–7], brain volume, and activation [8, 9], in older adults with and without cognitive impairment.

Vascular risk factors, such as hypertension, hypercholesterolemia, and diabetes mellitus, are associated with both the occurrence and progression of AD dementia [10–13]. It has also been found that vascular risk factors increase the risk of MCI [14, 15] and the risk of conversion from MCI to AD [16]. Li et al. [16] also reported that treatment (i.e., medication) of vascular risk factors was associated with a reduced risk of AD dementia, which suggests that active interventions for vascular risk factors might reduce the progression from MCI to AD dementia.

There is a growing body of evidence showing that regular physical activity has therapeutic and protective effects against dementia [17, 18] and cardiovascular disease [19] in older adults. Several studies have suggested that aerobic or resistance exercises have positive effects on vascular risk factors in healthy older adults, for example increases in high-density lipoprotein cholesterol (HDL-C) [20] as well as decreases in total cholesterol (TC), TC/HDL risk ratio, and triglyceride (TG) [21–23]. It is possible that improvements of metabolic profiles by exercise may lead to a decrease in the risk of dementia or vascular disease. However, it remains unclear whether exercise intervention affects vascular risk factors in older adults with MCI.

The identification and subsequent management of risk factors at the MCI stage could be an important strategy for preventing and delaying progression to AD. Considering the observed influence of the cardiovascular system and metabolic profile on the risk of developing dementia, it is important to know the potential benefits derived from exercise in terms of metabolomics. The purpose of this study was to investigate the effects of exercise intervention on vascular risk factors in older adults with MCI.

Participants and Methods

Participants

In this 12-month randomized controlled trial, subjects were randomly allocated to the exercise or education control group at the end of a baseline assessment. Study personnel involved in the collection of outcome measures were blinded to the randomization assignment. The Ethics Committee of the National Center for Geriatrics and Gerontology (Obu, Japan) approved the study protocol. The purpose, nature, and potential risks of the experiments were fully explained to the subjects, and all subjects gave written informed consent before participating in the study.

Subjects in this study were recruited from our volunteer databases, which included elderly individuals (65 years and over). Participants had to be community-dwelling adults aged 65 years and older to be included in the study. A total of 528 prospective subjects with a Clinical Dementia Rating (CDR) of 0.5 [24] or who complained of memory impairment were recruited in the first eligibility assessments. A total of 135 subjects responded to the second eligibility assessments. Thirty-five out of 135 subjects were excluded, and the 100 subjects

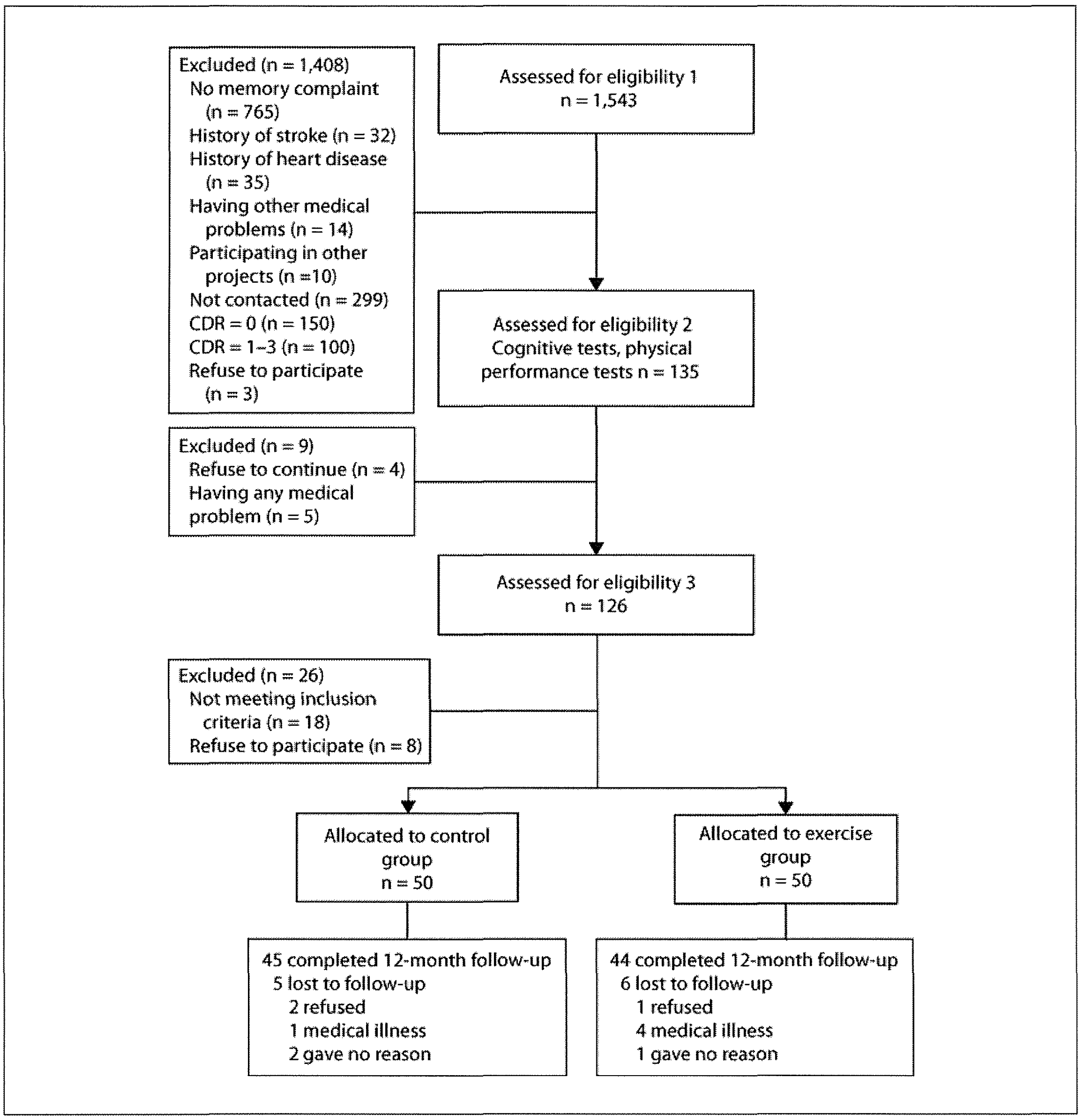

Fig. 1. Subject flow diagram from the initial contact through to study completion.

who remained met the definition of MCI using the Petersen criteria [3]. Exclusion criteria included a CDR of 0 or 1–3, a history of neurological, psychiatric, and cardiac disorders, and other severe health issues (i.e., recent myocardial infarction and unstable angina), uncontrolled hypertension, use of donepezil, impairments in basic activities of daily living, and participation in other research projects.

The Consolidated Standards of Reporting Trials (CONSORT) [25] diagram outlining the subject flow from the first contact to the study completion is shown in figure 1.

Interventions

The 12-month exercise program involved biweekly 90-min sessions with aerobic exercise, muscle strength training, postural balance retraining, and combined training. In addition, the exercise program included a focus on promoting exercise and behavior change. Two trained physiotherapists involved in geriatric rehabilitation conducted each intervention. Each supervised session began with a 10-min warm-up period and stretching exercise, followed by 20 min of muscle strength exercise. Then, the participants practiced aerobic exercise, postural balance retraining, and combined training for 60 min. For the aerobic exercise, participants underwent stair stepping and endurance walking. The mean intensity of the aerobic exercise was approximately 60% of the maximum heart rate.

Before and after each session of the program, the physiotherapists conducted a physical check of each participant. The participants were required to carry out daily home-based muscle strength exercises and walking, which were self-monitored using a booklet and pedometer based on the concept of promoting exercise and behavior change.

Subjects in the education control group attended three education classes about health promotion during the 12-month study period. The classes provided information regarding aging, healthy diet, oral care, brain image diagnosis, prevention of urinary incontinence, and health checks. However, the group did not receive specific information regarding exercise, physical activity, or cognitive health.

Anthropometry

Anthropometric measurements were obtained while the subjects were dressed in light clothing without shoes. Height (to the nearest 0.1 cm) and body weight (to the nearest 0.1 kg) were recorded. The body mass index (BMI) was calculated using the standard formula: weight (kg)/[height (m)^2].

Blood Markers and Blood Pressure

TC, HDL-C, TG, and glycosylated hemoglobin (HbA1c) were measured from blood samples, which were collected between 11 a.m. and 4 p.m. in a non-fasting state. The blood samples were kept at room temperature for 30 min to allow for clotting, then the samples were centrifuged for 15 min. Serum was harvested and stored at –25°C until analysis. Analyses were carried out centrally in one laboratory (Special Reference Laboratories, Tokyo, Japan). Serum samples were analyzed for TC, HDL-C, TG, and HbA1c. The TC/HDL-C ratio [26] was calculated as an index of lipid-associated coronary heart disease risk and is supported by both its superior predictive power compared with TC, LDL-C, or HDL-C levels and lower within-person variability [27]. Systolic and diastolic blood pressures were measured using a standard sphygmomanometer in the sitting position after a 5-min rest.

Physical Fitness

The participants' exercise capacity was quantitatively measured using the 6-min walking test (6MWT). The 6MWT is used to measure the maximum distance that a person can walk in 6 min [28]. Participants were instructed to walk as far as possible in 6 min along a 10-meter course, performed under the supervision of a physiotherapist. This study used the distance (in meters) in the 6MWT as a measure of physical fitness.

Statistical Analysis

Baseline characteristics were compared among groups using Student's t test for quantitative variables and the χ^2 test for qualitative variables. The intervention effects on all outcome measures were determined using two-way repeated measures ANOVA, with group (exercise, control) as a between-subjects factor and time (before training, after training) as a within-subjects factor. A probability of $p < 0.05$ was considered statistically significant. Post hoc comparisons were performed to test the differences in physical function variables between before and after the training in each group. The significance level of multiple comparisons was adjusted using the Bonferroni correction ($p < 0.025$; 0.05/2), and analyses were

Table 1. Baseline characteristics of the study subjects

	Exercise (n = 50)	Control (n = 50)	p value (t test)
Age, years	74.8 ± 7.4	75.8 ± 6.1	0.46
Men	25 (50)	26 (52)	0.84[a]
BMI	23.4 ± 3.4	22.9 ± 3.1	0.52
Educational level, years	10.9 ± 2.8	10.3 ± 2.3	0.29
Number of medications	2.5 ± 2.3	2.4 ± 2.2	0.89
GDS score	3.8 ± 3.1	3.3 ± 2.8	0.38
Physical performance			
Grip strength, kg	24.7 ± 8.1	23.5 ± 7.3	0.47
Timed up & go, s	8.8 ± 2.5	9.2 ± 2.1	0.37
Cognitive function			
MMSE score	26.8 ± 2.3	26.3 ± 2.7	0.30
ADAS-cog score	6.0 ± 2.7	6.5 ± 2.8	0.37

Values are means ± SD or n (%). GDS = Geriatric Depression Scale; MMSE = Mini-Mental State Examination; ADAS-cog = Alzheimer's Disease Assessment Scale-cognitive subscale. [a] χ^2 test.

performed using SPSS version 20.0 for Windows (SPSS Inc., Chicago, Ill., USA). To perform the intention-to-treat analysis, a single imputation was used for all outcome measures. Missing data values were estimated using mean values for each corresponding group [29].

Results

There were no significant differences in baseline characteristics between the exercise and control groups (table 1). Figure 1 shows the flow of participants from the time of screening to study completion at 12 months. Eighty-nine (exercise group, n = 44) subjects completed the 12-month follow-up. The mean adherence to the exercise program was 78.6%, and 34 subjects (68.0%) in the exercise group attended our intervention program with more than 80% adherence.

Table 2 depicts all fitness-related variables for the exercise and control groups before and after the training. No interaction effects between group and time were detected for body weight and BMI [F(1, 98) = 0.6, p = 0.43; F(1, 98) = 0.4, p = 0.51, respectively]. Both the exercise and control groups showed reduced body weight and BMI after the intervention compared with before the intervention (exercise, p < 0.001; control, p = 0.01).

No interaction effects between group and time were detected for systolic and diastolic blood pressure [F(1, 98) = 1.0, p = 0.31; F(1, 98) = 3.7, p = 0.06, respectively]. Both the exercise and control groups showed reduced systolic blood pressure after intervention (exercise, p = 0.02; control, p = 0.001), but no significant change in diastolic blood pressure between before and after the intervention was observed in both groups (exercise, p = 0.09; control, p = 0.9).

A statistically significant interaction effect between group and time was found for the TC level [F(1, 98) = 5.1, p = 0.03; fig. 2a]. Post hoc comparisons revealed that the exercise group had significantly reduced TC levels compared with baseline levels (p < 0.001); however, no significant reduction was found for the control group (p = 0.09). There were no interaction effects between group and time for other blood markers [TC/HDL-C risk ratio, F(1, 98) = 0.77, p = 0.38; HDL-C, F(1, 98) = 0.6, p = 0.25; TG, F(1, 98) = 0.2, p = 0.78; HbA1c, F(1, 98) = 0.05, p = 0.36]. Post hoc comparisons revealed that the exercise group had a significantly reduced TC/HDL-C risk ratio after exercise training compared with before exer-

Table 2. Fitness-related measurements according to group before and after the intervention (mean ± SD)

		Before	After	F-value 1. time effect 2. time × group	Partial η^2 1. time effect 2. time × group
Anthropometry					
Body weight, kg	exercise group	56.2 ± 9.6	55.2 ± 8.9**	$19.7^{\dagger\dagger}$	0.17
	control group	54.2 ± 8.8	53.5 ± 8.7*	0.6	0.006
BMI	exercise group	23.4 ± 3.3	22.9 ± 3.1**	$19.7^{\dagger\dagger}$	0.17
	control group	22.8 ± 3.1	22.5 ± 3.0*	0.4	0.004
Blood pressure					
Systolic, mm Hg	exercise group	144.6 ± 21.6	138.4 ± 20.3*	$17.8^{\dagger\dagger}$	0.15
	control group	142.4 ± 19.4	132.5 ± 17.5**	1.0	0.01
Diastolic, mm Hg	exercise group	74.6 ± 11.7	77.9 ± 11.1	0.24	0.014
	control group	75.1 ± 11.2	74.3 ± 9.2	3.7	0.036
Blood markers					
TC, mg/dl	exercise group	211.7 ± 36.2	193.6 ± 28.1**	$19.3^{\dagger\dagger}$	0.16
	control group	200.5 ± 34.6	194.7 ± 31.0	$5.1^{\dagger}$	0.05
TC/HDL-C risk ratio	exercise group	3.9 ± 1.0	3.7 ± 1.0**	$10.8^{\dagger\dagger}$	0.1
	control group	3.8 ± 0.9	3.7 ± 0.8	0.38	0.008
HDL cholesterol, mg/dl	exercise group	57.5 ± 16.0	55.6 ± 14.6	0.3	0.01
	control group	55.1 ± 13.2	55.2 ± 12.5	0.25	0.01
TG, mg/dl	exercise group	129.2 ± 64.7	131.8 ± 57.4	0.007	0
	control group	138.5 ± 91.5	134.7 ± 69.9	0.21	0.002
HbA1c, %	exercise group	5.6 ± 0.8	5.6 ± 0.9	1.1	0.01
	control group	5.4 ± 0.5	5.4 ± 0.4	0.05	0.001
Physical fitness					
6MWT distance, m	exercise group	378.0 ± 78.4	445.9 ± 97.8**	$81.5^{\dagger\dagger}$	0.45
	control group	363.5 ± 63.0	402.9 ± 70.7**	$5.7^{\dagger}$	0.06

* Significant difference between before and after the training within the group (Bonferroni, $p < 0.025$).
** Significant difference between before and after the training within the group (Bonferroni, $p < 0.005$).
†† $p < 0.01$; † $p < 0.05$.

cise training (p = 0.004), but no significant reduction was found for the control group (p = 0.09). There were no significant changes in HDL-C, TG, and HbA1c between before and after the intervention in both the exercise and control groups.

6MWT, our measure of physical fitness, showed significant interaction effects between group and time [F(1, 98) = 5.7, p = 0.02; fig. 2b] and was significantly increased in both the exercise and control groups compared with before the intervention (exercise, $p < 0.001$; control, $p < 0.001$).

Discussion

This study found that exercise intervention resulted in positive changes of blood markers, namely TC and TC/HDL-C levels, among older adults with MCI. Our baseline values were normal for TG and HDL-C, and borderline high for TC [30]. Numerous studies have shown that exercise improves lipid profiles among older adults. Indeed, a meta-analysis concluded that exercise could improve lipid profiles, including reducing TC and TC/HDL-C levels [31]. The multicomponent exercises in our intervention involved mainly aerobic exer-

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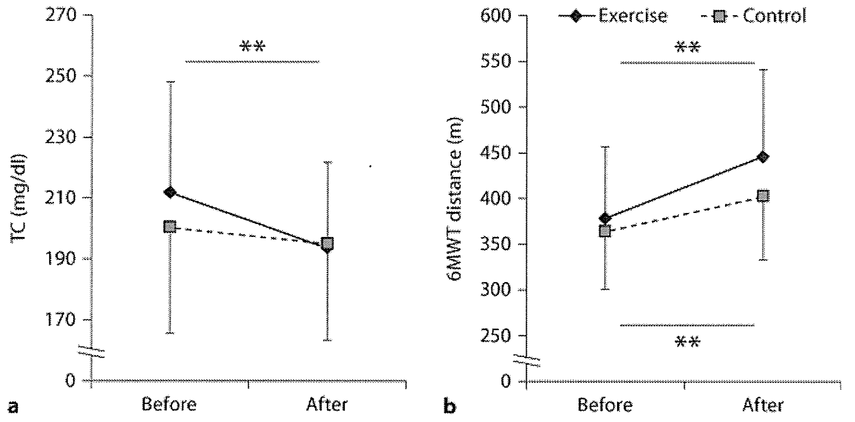

Fig. 2. The average values of TC (**a**) and 6MWT distance (**b**) in the exercise and control groups before and after the intervention. ** Significant difference between before and after the training within the group (Bonferroni post hoc test, $p < 0.005$).

cise. This type of exercise has been suggested to have positive effects on lipid profiles among older adults with coronary artery disease [32] or type 2 diabetes [33] as well as among healthy older adults [34]. Our study is the first to reveal the effectiveness of exercise intervention on vascular risk factors in older adults with cognitive impairment. Moreover, cardiorespiratory fitness also improved as a result of the increase in the 6MWT distance after exercise intervention, which is in line with previous studies reporting that exercise intervention improved cardiorespiratory functionality in healthy older adults, potentially counteracting the documented age-related decline in peak oxygen uptake [22, 23]. Previous studies have reported associations between habitual physical activity levels, increased endurance capacity, and/or chronic exercise programs and improvements in lipoprotein profiles in elderly subjects [35, 36]. In the present study, improved cardiorespiratory fitness might contribute to increased physical activity and positive changes in lipid metabolism.

From a metabolomic point of view, exercise intervention may be useful for dementia prevention in older adults with MCI. It has been reported that higher serum levels of TC lead to future cognitive decline and risk of cognitive impairment [37, 38]. It has also been reported that hypercholesterolemia independently increases the risk of conversion from MCI to AD [16]. Improved cardiorespiratory fitness and lipid metabolism may prevent vascular pathologies such as atherosclerosis. Furthermore, cholesterol is known to interact with, and modulate the generation of, Aβ, which alters cholesterol dynamics in neurons leading to tauopathy [39]. In addition, hypercholesterolemia promotes Aβ production by activating the activity of β- and γ-secretases [40]. The increased Aβ burden resulting from hypercholesterolemia may ultimately promote the development of AD [16]. The Aβ-modulating role of cholesterol may contribute to cognitive dysfunction, although conclusive evidence of the pathophysiological mechanism in dyslipidemias has not been provided yet [39]. In the current study, we also found that decreased TC levels were associated with an improvement in logical memory scores after exercise intervention [unpubl. data]. Therefore, exercise intervention may prevent cognitive decline and the incidence of dementia in older adults with MCI by improving cholesterol metabolism and risk factors (i.e., TC and TC/HDL-C levels) in older adults with MCI.

Cholesterol is not only a risk factor for cognitive impairment, but is also regarded as a vascular risk factor in such diseases as coronary heart disease and cerebrovascular disease [41]. It has been reported that TC is positively associated with ischemic heart disease mortality in both middle- and old-aged patients [42]. Independent of the mechanism underlying lipid changes, a reduction of 1% in TC level has been shown to reduce the risk for coronary artery disease by 2% [43], which implies that our exercising participants have reduced their risk of coronary artery disease by approximately 17%. Additionally, there is a growing body of evidence showing that regular physical activity has therapeutic and protective effects against cerebrovascular disease in older adults [19]. Exercise intervention may have the potential to prevent incidences of vascular disease and related mortality in older adults with MCI. Overall, exercise is a beneficial and inexpensive practice that is associated with numerous benefits for cognitive and metabolic health with minimal adverse effects.

Study Limitations

There are several limitations to the current study. First, blood samples were collected in a non-fasting state. Although it has been reported that lipoprotein and apolipoprotein levels are not considerably different between fasting and non-fasting states, with the exception of TG, a fasting sample is preferred for precise assessment and management of cardiovascular risk [44]. Second, the intervention of this study lacked nutrient intake assessment and dietary control. It is possible that changes in nutrient intake contributed to decreases in body weight, systolic blood pressure in both groups, and unchanged HDL-C levels, which have been shown to decrease with low total and saturated fat diets [45]. To ascertain that the observed changes were due to exercise rather than other possible factors, a randomized controlled trial with control of nutrient intake in older adults with cognitive impairment and abnormal metabolic profiles, such as metabolic syndrome, should be conducted.

Conclusions

We investigated the effects of exercise intervention on vascular risk factors in older adults with MCI. The main finding of this study is that exercise intervention reduced TC levels and TC/HDL-C risk ratios among older adults with MCI. Reduction of these vascular risk factors may contribute to reduced cognitive decline and prevention of dementia, vascular disease, and related mortality in the future.

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Disclosure Statement

The authors have no conflict of interest to declare.