

## ORIGINAL ARTICLE

## EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

# Increasing light physical activity helps to maintain cognitive function among the community-dwelling oldest old population: a cross-sectional study using actigraph from the Arakawa 85+ study

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Received: 27 January 2020

Revised: 13 May 2020

Accepted: 23 May 2020

**Aim:** To investigate the influence of replacing sedentary time with physical activity on cognitive function using an isotemporal substitution model in a population of community-dwelling oldest old.

**Methods:** This cross-sectional study included residents of the Arakawa ward, Tokyo, who were part of a prospective cohort from the Arakawa 85+ study. We measured physical activity in 136 participants using a triaxial actigraph. Cognitive function was measured using the Addenbrooke's Cognitive Examination-III and participants were divided into a "cognitive decline group" (Addenbrooke's Cognitive Examination-III  $\leq 88$ ) and "cognitive maintain group" (Addenbrooke's Cognitive Examination-III  $\geq 89$ ). Physical activity was divided into three categories: sedentary behavior ( $\leq 1.5$  metabolic equivalents), light physical activity ( $>1.5$  to  $<3.0$  metabolic equivalents), and moderate-to-vigorous physical activity ( $\geq 3$  metabolic equivalents). Using an isotemporal substitution approach, we applied multiple logistic regression analysis to demonstrate the association between cognitive function and replacing 30 min/day of sedentary behavior with an equal period of light physical activity. Covariates included age, education and the Center for Epidemiologic Studies Depression Scale.

**Results:** Our findings showed that in men, replacing 30 min of sedentary behavior per day with light physical activity was associated with a 1.47-fold increase in the odds of maintaining cognitive function. An association between physical activity and cognitive function was not observed in female participants.

**Conclusions:** Our results indicate that substituting sedentary behavior with light physical activity could be helpful in maintaining cognitive function in community-dwelling oldest old men. These results highlight the importance of behavioral changes to promote cognition. *Geriatr Gerontol Int* ••; ••: ••–•• *Geriatr Gerontol Int* 2020; ••: ••–••.

**Keywords:** actigraph, cognitive function, isotemporal substitution model, oldest old, physical activity.

## Introduction

Japan is a rapidly aging society, with its average life expectancy reaching 87.32 years old for women and 81.25 years old for men as of 2018. The term "oldest old" was first proposed by Suzman and Riley in the mid-1980s, calling for a need to focus on this population,<sup>1</sup> which consists of people  $>85$  years. Along with increased life expectancy, a rapid increase in the oldest old population is one of the biggest structural changes facing modern society. According to the World Health Organization (WHO), the worldwide oldest old population is expected to increase by 351% from 2010 to 2050. In Japan, this population has tripled from 1.58 million in 1995 to 4.89 million in 2015. According to a large cohort study, morbidity caused by dementia is 18%–38% in populations  $>85$  years old.<sup>2</sup>

Much has been reported regarding daily physical activity (PA) of the aged population. Generally, PA declines and sedentary

behavior (SB) (i.e. watching television, reading books and using the computer) increases with age,<sup>3</sup> with deterioration being particularly noticeable in aged populations with dementia.<sup>4</sup> One systematic review showed that PA alleviates cognitive decline and dementia incidence among people aged  $>60$  years old.<sup>5</sup> However, another systematic review reported that interventions with PA do not contribute to an improvement in cognitive function.<sup>6</sup> Therefore, the causal inference between PA and cognitive function is controversial and has yet to be clarified.

In the WHO guidelines, PA is recommended to adults to reduce the risk of cognitive decline.<sup>7</sup> In particular, the WHO recommends 150 min of moderate-intensity levels of weekly PA for people aged  $\geq 65$ , but does not make any special reference to the oldest old population. Similarly, the Japanese Ministry of Health Labour and Welfare recommends 40 min of any kind of daily PA,<sup>8</sup> but no recommendations have been made exclusively for the oldest old population.

Most studies supporting the WHO and Japanese guidelines have measured PA levels based on self-reported questionnaires, which are less reliable in the aged population due to recording bias, memory difficulty and underreporting of SB.<sup>9</sup> To solve this problem, actigraphy has been recently utilized as an objective alternative for self-reported questionnaires. Actigraphs use three-dimensional acceleration data to evaluate daily PA accurately.

To the best of our knowledge, no study has examined the relationship between cognitive function and PA using actigraphy among the oldest old population. The Newcastle 85+ study<sup>10</sup> used actigraphy to measure PA in the oldest old population and reported a correlation between objective and subjective activity level; however, the association with PA and cognitive function was not investigated. Actigraph research has been implemented in populations aged <85 years, and results have indicated that light PA prevents cognitive impairment.<sup>11</sup> These results may also be consistent with our study on oldest old.

Previous studies have attempted to elucidate the protective factors of cognitive function in the community-dwelling oldest old population; however, the interdependence between different PAs has yet to be fully considered. A day is limited to 24 h, and to have time to perform one activity, it is necessary to reduce another activity.<sup>12</sup> The “isotemporal substitution model” is a methodology that “addresses the more practical question of the potential relationship of replacing time spent in one activity type to [sic] time in another activity.”<sup>13</sup> Because this methodology conceptually replaces one activity with another, its results can be easily interpreted and implemented in actual clinical and community settings. Although there are studies of the relationship between PA and physical function in older people,<sup>12</sup> to date, no study has examined the relationship between PA and cognitive function, nor in the oldest old population. Therefore, we aimed to examine the impact of the replacement of SB with PA on cognitive function in the community-dwelling oldest old population, and to clarify the activity level required to maintain cognitive function.

## Methods

### Baseline data collection

#### Participants

Participants in our cohort were recruited from the Arakawa ward, which has an approximate population of 210 000 and is located in north-eastern Tokyo. To participate, subjects were required to provide consent for the Arakawa 85+ study and consent to wearing an actigraph. Participants with alcohol abuse and physical disability were excluded.

We first sent Arakawa 85+ study questionnaires, which asked about lifestyle, geriatric care condition, and physical, psychological and social determinants of health, to the participants' residences. In-depth individual interviews were conducted at a later date by a trained surveyor (i.e., medical doctor, nurse or psychologist) in a public facility or in participants' homes, depending on accessibility. The Addenbrooke's Cognitive Examination (ACE)-III was used to measure cognitive function, with a score of  $\leq 88$  indicating mild cognitive impairment.<sup>14</sup> Using this cut-off point, we classified ACE-III results into the “cognitive decline group” (ACE-III  $\leq 88$ ) and “cognitive maintain group” (ACE-III  $\geq 89$ ). The Center for Epidemiologic Studies Depression Scale (CES-D)<sup>15</sup> was used to measure depressive symptoms. In addition to mental health variables, physical health variables, such as body mass index and Barthel index,<sup>16</sup> which is a typical evaluation for activities of daily living with a score of  $\geq 85$  indicating independence, were also evaluated. At the end of the interviews, the diagnosis of dementia was

also assessed by a psychiatrist. We used the Diagnostic and Statistical Manual of Mental Disorders 5 criteria to diagnose dementia.<sup>17</sup>

After the interviews, we sent actigraph units (GT3X; ActiGraph, Pensacola, FL, USA) to participants' homes. Participants wore the unit on their waist belt during sleeping and waking hours for seven consecutive days, removing it only for bathing. Sleeping time was included in the 24-h wearing time. Data were downloaded using special analysis software (ActiLife v6.13.3), and a file of the participants' PA record was obtained. Epoch lengths were set for 60 s. We used the counts per minute (cpm) intensity threshold to divide hourly PA into three levels:  $<100$  cpm for SB ( $\leq 1.5$  metabolic equivalents [METs]), 100–1039 cpm for light PA (LPA;  $>1.5$  to  $<3.0$  METs) and  $\geq 1040$  cpm for moderate-to-vigorous PA (MVPA;  $\geq 3$  METs).<sup>18</sup> Non-wearing time was measured when zero count (cpm) continued for at least 60 min, and total wear time was calculated as 24 h minus non-wearing time.<sup>19</sup> We included participants for whom we successfully obtained data for more than four consecutive days and  $>600$  min per day.<sup>20</sup> PA levels were calculated as the total PA minutes divided by each day that the actigraph was worn (min/day); this calculation was performed for each activity level (SB, LPA and MVPA).

### Statistical analyses

In this single arm cross-sectional study, as dementia prevalence and associated factors (e.g., obesity, type 2 diabetes and cardiovascular disease) differs by sex,<sup>21</sup> we stratified our participants accordingly, in addition to presenting results from all participants.

PA levels (min/day) for the three activity categories (SB, LPA and MVPA) were used as variables to measure PA. For demographic data stratified by sex, continuous data are expressed as mean  $\pm$  standard deviation. Student's *t*-test and Mann-Whitney *U*-tests were used to compare the two subgroups. Categorical data were analyzed using the chi-squared test and presented as *n* (%). We used three multiple logistic regression models to examine the relationship between SB, PA and its replacement, and cognitive function: single factor, partition and isotemporal substitution models.<sup>13</sup> The primary outcome variable was a binary ACE-III score with a cut-off value of 88/89. As explanatory variables, average daily minutes for the three activity categories were calculated using 30 min as one unit for simplification. Covariates were selected according to past studies:<sup>22</sup> age, years of education and depression (i.e., CES-D). We measured PA over 24 h, but this does not take into account sleep time. Therefore, we performed a sensitivity analysis excluding 12.00 to 06.00 h as an assumed sleep time, as has been done previously.<sup>23</sup> Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each variable. Analyses were done using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) with a statistical significance level of  $P < 0.05$ . The outline of the three models is as follows.

#### Single factor model

Time units spent performing each activity category, total time wearing the actigraph, and covariates were entered into the model, and the overall effect of each activity on cognitive outcome was examined.

#### Partition model

All time units spent performing any of the activity categories and covariates were entered into the same model, and the independent effects of each behavioral variable were examined.

### Isotemporal substitution model

One of the three activity categories were excluded from the regression model. Two activity categories, total time wearing actigraph and covariates were entered in to a model. For example, to examine the effect of substituting SB with LPA, time units spent performing either LPA or MVPA, total time wearing actigraph and covariates were entered into the regression model. If, in this example, we focus on the change in cognitive function per LPA time units increase, MVPA and wearing time are equivalent to being fixed in this model. The interpretation of the regression coefficient of LPA is its effect on cognitive function when 30 min of SB is substituted with 30 min of LPA.

### Ethical considerations

We performed this study in accordance with the principles set forth in the Declaration of Helsinki and under the approval of the Keio University Hospital Institutional Review Board with written and oral consent. We registered this study in the University Hospital Medical Information Network (UMIN ID: 000019088) as an ongoing clinical study.

## Results

### Recruitment

Among 2927 residents aged 85–87 years as of January 1, 2016, we sent our questionnaire to 2443 persons who survived as of the sending dates (October 16, 2017 and February 19, 2018). Among these, 233 underwent in-depth interviews by July 2018 (193 conducted in public facilities and 40 at home). Among the interviewed participants, 154 consented to the actigraph study. Among these, 18 were excluded due to declining use of actigraph or death, with 136 completing the actigraph study.

### Demographic data

Demographic data of our participants are shown in Table 1. Among the 136 participants, there was no statistical difference in age, education years, CES-D, ACE-III, body mass index or actigraph wear percentage between male and female participants. A greater number of female than male participants lived alone due to divorce or bereavement. Men were more sedentary, with significantly lower total LPA time than women were.

### Statistical analysis results

Table 2 shows the average minutes per day spent performing each activity category in the cognitive decline and maintain groups across male and female subgroups. Men in the high ACE-III score group spent more time performing higher intensity activities compared with those in the low ACE-III score group. However, in women, the tendency was reversed—those with low ACE-III scores spent more time performing high-intensity activities.

Table 3 shows the association between cognitive decline and time units spent performing each activity category, stratified by sex. In the single factor model for the male subgroup, being in the cognitive maintain group was negatively correlated with a longer SB time (beta coefficient (B) =  $-0.34$ , OR = 0.71, 95% CI = 0.54, 0.94), and positively correlated with a longer LPA time (B = 0.37, OR = 1.45, 95% CI = 1.06, 1.99). In the partition model, LPA was independently associated with the cognitive maintain group (B = 0.342, OR = 1.41, 95% CI = 1.05, 1.90). In the male isotemporal substitution model, substituting 30 min per day of SB

with LPA resulted in a 1.47-fold increase in the odds of maintaining cognitive function (B = 0.385, 95% CI = 1.06, 2.04). This association was not observed when substituting SB with MVPA. None of the above-mentioned associations, nor any other associations, were observed in women. We also performed a sensitivity analysis using only data from 06.00 to 12.00 h, which is presented in Table S1.

## Discussion

This study examined the effect of replacing SB with PA on cognitive function using an isotemporal substitution model in a cohort of community-dwelling oldest old. In oldest old men, replacing 30 min of SB per day with LPA significantly increased the odds of maintaining cognitive function. No significant association was found in women.

Although our study used an isotemporal substitution model, it is consistent with past studies in that it demonstrates that longer SB and shorter LPA leads to deteriorating cognitive function.<sup>11,24</sup> It has been reported that casual daily activities such as housework are sufficient to prevent cognitive deterioration.<sup>25</sup> Reports from actual community settings have shown an association between active social participation and a lower risk of cognitive decline.<sup>26</sup> Therefore, long-lasting low-intensity activities that can be easily performed in daily life are better suited to maintain cognitive levels in older people than short-term high-intensity aerobic exercises. This is even more critical in the oldest old population, where physical function is decreasing.

Although the mechanism underlying the association between PA and cognitive function has yet to be identified, previous studies have reported the following theories, i.e., (i) PA decreases physical and psychological risk factors for dementia, such as hypertension, obesity, stroke and depression (more specifically, it has been reported that PA enhances brain-derived neurotrophic factors in the hippocampus, enhancing angiogenesis, neurogenesis and synapse generation),<sup>27</sup> and (ii) social isolation is a known risk factor for dementia,<sup>22</sup> and increasing SB leads to social isolation.<sup>28</sup> Further study is needed to clarify the comprehensive factors involved in this association.

A previous study has shown that MVPA is associated with a reduced decline in cognitive ability in community-dwelling older adults.<sup>11</sup> However, that cohort was different from ours as the subjects of the previous study were 74.5 years, whereas the subjects in the present study were 88.0 years, and it is assumed that the subjects in the previous study had relatively better physical ability. Therefore, MVPA may have affected cognitive function in previous studies with younger populations, but not our older cohort, likely due to physical function.

For PA in women, SB was shorter and LPA and MVPA were longer than in men. In the female subgroup, PA was not statistically associated with ACE-III score. The possible reasons are as follows, i.e., (i) there are many cognitive activities that women can perform even while sitting (talking with friends, hobbies such as knitting, housework, etc.), and (ii) in Japan, women tend to spend more time on housework than men (44 min/week for men and 328 min/week for women),<sup>29</sup> so there are many original low-intensity activities that are not easily affected by cognitive decline.

One strength of our study was that we objectively measured PA using actigraphs. Most previous studies utilized self-reported PA, allowing for the potential for recall bias. Furthermore, ours was the first study to use an isotemporal substitution model exclusively for oldest old participants.

**Table 1** Characteristics of study participants

	Total <i>n</i> = 136	Male <i>n</i> = 68 (50.0%)	Female <i>n</i> = 68 (50.0%)	<i>P</i>
Age, years (mean ± SD)	88.0 ± 1.0	88.0 ± 1.0	88.0 ± 0.9	0.751 <sup>†</sup>
Living condition, <i>n</i> (%)				
Living alone	47 (34.6)	13 (19.1)	34 (50.0)	<0.001 <sup>§*</sup>
Living with others	88 (64.7)	55 (80.9)	33 (48.5)	
Nursing home	1 (0.7)	0 (0.0)	1 (1.5)	
Education, years (mean ± SD)	10.6 ± 2.7	11.1 ± 3.1	10.1 ± 2.1	0.152 <sup>†</sup>
Marital status, <i>n</i> (%)				
Married	57 (41.9)	49 (72.1)	8 (11.8)	<0.001 <sup>§*</sup>
Divorce/bereavement	70 (51.4)	18 (26.5)	52 (76.5)	
Never	9 (6.6)	1 (1.5)	8 (11.8)	
Mental health				
CES-D (mean ± SD)	7.6 ± 6.7	7.5 ± 5.9	7.7 ± 7.5	0.642 <sup>†</sup>
ACE-III (mean ± SD)	81.9 ± 9.8	81.1 ± 11.0	82.8 ± 8.5	0.639 <sup>†</sup>
Diagnosis of dementia, <i>n</i> (%)	2 (1.47)	2 (2.94)	0 (0.0)	
Physical health				
BMI (mean ± SD)	22.6 ± 3.3	22.8 ± 3.1	22.4 ± 3.4	0.243 <sup>†</sup>
Barthel index	98.2 ± 5.7	97.9 ± 7.2	98.4 ± 3.7	0.401 <sup>†</sup>
Actigraph wear time, hours (mean ± SD)	18.4 ± 2.7	18.5 ± 2.9	18.4 ± 2.5	0.863 <sup>‡</sup>
Physical activity levels (mean ± SD [%])				
SB (min/day)	826.4 ± 145.6 (74.6)	854.7 ± 144.9 (76.9)	798.2 ± 141.9 (72.4)	0.023 <sup>‡,*</sup>
LPA (min/day)	249.3 ± 83.8 (22.5)	228.0 ± 73.0 (20.5)	270.5 ± 88.9 (24.5)	0.003 <sup>‡,*</sup>
MVPA (min/day)	31.6 ± 28.3 (2.9)	29.0 ± 26.3 (2.6)	34.1 ± 30.2 (3.1)	0.289 <sup>‡</sup>

ACE-III, The Addenbrooke's Cognitive Examination-III; BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; LPA, light physical activity; MVPA, moderate-to-vigorous physical activity; SB, sedentary behavior.

\**P* < 0.05.

<sup>†</sup>Mann-Whitney *U*-test.

<sup>‡</sup>Student *t*-test.

<sup>§</sup>Chi-squared test.

Our study had several limitations. First, our sample size was not large enough to be representative of the population of Japan, thus the generalizability of our study is limited. Second, most of our participants were very healthy, lived independently in the community, and had a lower incidence of dementia than those of a similar age. This was indicated by a high mean Barthel index score of  $98.2 \pm 5.7$  points and a prevalence of dementia of 1.47%, which is very low compared with the previous studies that have found the prevalence of dementia for those aged  $\geq 85$  years to be

between 18% and 38%.<sup>2</sup> Third, due to our cross-sectional study design, cause-effect relationships cannot be inferred. Therefore, interventional studies or prospective cohorts based on our current findings are warranted. Fourth, we did not consider the length of sleeping time. In an attempt to address this, we performed a sensitivity analysis under the assumption that participants were asleep from 12.00 to 06.00 h (i.e., using data only for 06.00 h to 12.00 h), and the results were almost the same. These results confirmed that the data we obtained were sufficiently robust.

**Table 2** Minutes per day performing each activity category in the cognitive decline and cognitive maintain group

	<i>n</i>	SB (min/day)	<i>P</i>	LPA (min/day)	<i>P</i>	MVPA (min/day)	<i>P</i>
Male							
ACE-III $\leq 88$ (cognitive decline group)	54	859.1 ± 149.2	0.363 <sup>†</sup>	217.6 ± 67.5	0.020 <sup>‡,*</sup>	28.1 ± 28.0	0.184 <sup>†</sup>
ACE-III $\geq 89$ (cognitive maintain group)	14	837.4 ± 130.3		268.2 ± 81.6		32.5 ± 18.5	
Female							
ACE-III $\leq 88$ (cognitive decline group)	50	788.6 ± 150.0	0.357 <sup>†</sup>	280.8 ± 94.2	0.111 <sup>‡</sup>	36.4 ± 32.7	0.370 <sup>†</sup>
ACE-III $\geq 89$ (cognitive maintain group)	18	824.8 ± 116.0		241.8 ± 66.2		27.7 ± 21.2	

ACE-III, Addenbrooke's Cognitive Examination-III; LPA, light physical activity; MVPA, moderate-to-vigorous physical activity; SB, sedentary behavior.

\**P* < 0.05.

<sup>†</sup>Mann-Whitney *U*-test.

<sup>‡</sup>Student *t*-test.

**Table 3** Associations between ACE-III score and SB, LPA and MVPA using single factor, partition, and isotemporal substitution models by logistic regression analysis

Models	SB				LPA				MVPA			
	B	OR	95% CI	p	B	OR	95% CI	p	B	OR	95% CI	p
Male												
(i) Single factor	-0.34	0.71	(0.54, 0.94)	0.017 *	0.37	1.45	(1.06, 1.99)	0.019 *	0.146	1.16	(0.56, 2.41)	0.696
(ii) Partition	-0.069	0.93	(0.81, 1.07)	0.332	0.342	1.41	(1.05, 1.90)	0.025 *	-0.167	0.85	(0.35, 2.06)	0.713
(iii) Isotemporal substitution	Dropped				0.385	1.47	(1.06, 2.04)	0.021 *	-0.119	0.89	(0.36, 2.17)	0.793
	Replace SB				Dropped				-0.543	0.58	(0.21, 1.64)	0.305
	Replace LPA								Dropped			
	Replace MVPA	-0.197	0.82	(0.49, 1.37)	0.452	0.187	1.21	(0.67, 2.18)	0.536			
Female												
(i) Single factor	0.138	1.15	(0.9, 1.47)	0.266	-0.21	0.81	(0.59, 1.12)	0.201	-0.096	0.91	(0.48, 1.70)	0.765
(ii) Partition	-0.026	0.98	(0.83, 1.15)	0.758	-0.281	0.76	(0.53, 1.08)	0.122	0.156	1.17	(0.52, 2.61)	0.702
(iii) Isotemporal substitution	Dropped				-0.255	0.78	(0.53, 1.14)	0.19	0.182	1.20	(0.56, 2.57)	0.64
	Replace SB				Dropped				0.444	1.56	(0.56, 4.33)	0.394
	Replace LPA	0.259	1.30	(0.88, 1.90)	0.186				Dropped			
	Replace MVPA	-0.167	0.85	(0.40, 1.81)	0.666	-0.419	0.66	(0.24, 1.81)	0.419			

All models are adjusted for age, education years, and score on the Center for Epidemiologic Studies Depression Scale (CES-D).

Before the regression models, all physical activity variables were divided by a constant of 30 so that a 1-unit increase in the behavior represented an increase of 30 min/day of the given behavior.

ACE-III, Addenbrooke's Cognitive Examination-III; LPA, light physical activity; MVPA, moderate-to-vigorous physical activity; SB, sedentary behavior.

B, beta coefficient; CI, confidence interval; OR, odds ratio.

\*  $P < 0.05$ .

Lastly, cognitive levels during SB depend on what activity the individual is doing,<sup>30</sup> however, this cannot be measured with actigraphy.

As the first study to measure PA in the community-dwelling oldest old population objectively, we revealed that substituting 30 min of SB with LPA was protective against cognitive impairment in men. This result is useful in that it sends a concrete message to community-dwelling oldest old men about the importance of behavioral changes on cognition. Further study on the oldest old population is needed to identify clinical features related to the association between PA and cognitive function, such as biomarkers and brain imaging, and to investigate how the current PA level influences future cognitive function.

## Acknowledgements

We thank the participants and their families for their time and assistance. We also thank: Taiichirou Nishikawa, the Mayor of Arakawa City; Takashi Kataoka, Director of Welfare Division; Chie Tanii and Yumiko Hori, Director of the Welfare for the Elderly Section; Hiroto Mizuno, Yuichi Ozawa and Shunichi Kojima, staff members of the Welfare for the Elderly Section (sampling/analyzing basic resident registry data); Dr. Yuko Oguma, Sports Medicine Research Center, Graduate School of Health Management, Keio University; Dr. Ayano Takeuchi and Dr. Yasunori Sato, Department of Preventive Medicine and Public Health, Keio University School of Medicine; Members of the Keio University Arakawa 85+ study team: clinical psychologists Maiko Kiyohara and Ayaka Morimoto; and research secretaries Chiaki Kojima and Yukiko Miyasaka. This work was supported by Keio Research Grants for Global Initiative Research Projects (grant number SKCL000216), the Taiyo Life Welfare Foundation, the Mitsui Sumitomo Insurance Welfare Foundation and The Inokashira Hospital Grants for Psychiatry Research (grant number IHGPR2018-04).

## Disclosure statement

HN received honoraria for lectures from Sumitomo Dainippon Pharma, Mochida Pharmaceutical, Otsuka Pharmaceutical, and Mitsubishi Tanabe Pharma. MM received grants and/or speaker's honoraria from Asahi Kasei Pharma, Astellas Pharma, Daiichi Sankyo, Sumitomo Dainippon Pharma, Eisai, Eli Lilly, Fuji Film RI Pharma, Janssen Pharmaceutical, Kracie, Meiji-Seika Pharma, Mochida Pharmaceutical, Merck Sharp and Dohme, Novartis Pharma, Ono Pharmaceutical, Otsuka Pharmaceutical, Pfizer, Shionogi, Takeda Pharmaceutical, Mitsubishi Tanabe Pharma, and Yoshitomi Yakuhin. All other authors declare that they have no conflicts of interest. HN has received research support from the Ministry of Education, Culture, Sports, Science and Technology, Japan Society for the Promotion of Science, Daiwa Securities Health Foundation, Unvers Foundation, Taiyo Welfare Foundation, and grants or speaker's honoraria from Dainippon-Sumitomo Pharma, Mochida Pharmaceutical, Otsuka Pharmaceutical and Tanabe Mitsubishi Pharma within the past 3 years. YE has received grants from Mitsubishi Foundation and Daiwa Securities Health Foundation within 3 years. MT has received research support from the Ministry of Education, Culture, Sports, Science and Technology, Japan Society for the Promotion of Science within the past 4 years. MM has received grants and/or speaker's honoraria from Asahi Kasei Pharma, Astellas Pharmaceutical, Daiichi Sankyo, Dainippon-Sumitomo Pharma, Eisai, Eli Lilly, Fuji Film RI Pharma, Janssen Pharmaceutical, Kracie, Meiji-Seika Pharma, Mochida

Pharmaceutical, MSD, Novartis Pharma, Ono Yakuhin, Otsuka Pharmaceutical, Pfizer, Shionogi, Takeda Yakuhin, Tanabe Mitsubishi Pharma, and Yoshitomi Yakuhin, and research funding from Nishikawa Sangyo, Otsuka Pharmaceutical, MSD, Meiji-Seika Pharma, and Shionogi & Co., Ltd. within the past 3 years.

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## Supporting information

Additional supporting information may be found in the online version of this article at the publisher's website:

**Table S1** Associations between ACE-III score and SB, LPA, and MVPA using single factor, partition, and isotemporal substitution models by logistic regression analysis (using data only for 6 AM to 12 PM as a sensitivity analysis)

**How to cite this article:** Suzuki K, Niimura H, Kida H, et al. Increasing light physical activity helps to maintain cognitive function among the community-dwelling oldest old population: a cross-sectional study using actigraph from the Arakawa 85+ study. *Geriatr. Gerontol. Int.* 2020;1–6. <https://doi.org/10.1111/ggi.13967>