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Association of step counts with cognitive function in apparently healthy middle-aged and older Japanese men

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ABSTRACT

Background: Increasing physical activity may prevent cognitive decline. Previous studies primarily focused on older adults and used self-reported questionnaires to assess physical activity. We examined the relationship between step count, an objective measure of physical activity, and cognitive function in community-based middle-aged and older Japanese men.

Methods: The Shiga Epidemiological Study of Subclinical Atherosclerosis randomly recruited community-dwelling healthy men aged 40–79 years from Shiga, Japan, and measured their step counts over 7 consecutive days using a pedometer at baseline (2006–2008). Among men who returned for follow-up (2009–2014), we assessed their cognitive function using the Cognitive Abilities Screening Instrument (CASI) score. We restricted our analyses to those with valid 7-day average step counts at baseline and those who remained free of stroke at follow-up ($n = 676$). Using analysis of covariance, we calculated the adjusted means of the CASI score according to the quartiles of the average step counts.

Results: The mean (standard deviation) of age and unadjusted CASI score were 63.8 (9.1) years and 90.8 (5.8), respectively. The CASI score was elevated in higher quartiles of step counts (90.2, 90.4, 90.6, and 91.8 from the lowest to the highest quartile, respectively, [p for trend = 0.004]) in a model adjusted for age and education. Further adjustment for smoking, drinking, and other cardiovascular risk factors resulted in a similar pattern of association (p for trend = 0.005).

Conclusion: In apparently healthy middle-aged and older Japanese men, a greater 7-day average step count at baseline was associated with significantly higher cognitive function score.

1. Introduction

Dementia is a rapidly growing global public health problem, with the number of patients increasing yearly (GBD, 2019 Dementia collaborators, 2019). A 2017 report by the Organization for Economic Cooperation and Development (OECD) revealed that Japan has the highest prevalence of dementia per 1,000 population at 23.3, compared to an average of 14.8 in 35 OECD member countries (OECD, 2017). Japan's Ministry of Health, Labor, and Welfare reports that by 2025, the number of people with dementia will reach 7 million, accounting for approximately one in five individuals ≥ 65 years (Cabinet Office, 2017).

The 2019 World Health Organization (WHO) guidelines on risk reduction in cognitive decline and dementia recommended lifestyle behaviors, including increase in physical activity, to delay or prevent cognitive decline and dementia (WHO, 2019). Previous observational epidemiological studies using self-reported physical activity assessments

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reported that physical activity contributes to the prevention of cognitive decline and dementia (Abbott et al., 2004; Kishimoto et al., 2016; Sofi et al., 2011). However, self-reported physical activity often suffers from recall and response bias, and thus measurement error. Therefore, in previous studies using subjective questionnaires, the associations with cognitive function were inconsistent (Chang et al., 2010; Gross et al., 2017; Sablina et al., 2017). Step counts are a direct and objective measure of physical activity; therefore, a reliable measure of physical activity in daily life (Bassett et al., 2017). Previous observational studies from Western countries that investigated step counts and cognitive function in older adults found a preventive effect (Calamia et al., 2018; Rabin et al., 2019). One study showed that step count may protect against cognitive function in old Asians (Chen et al., 2020), while there is also a report from Japan that found no association (Yoshiuchi et al., 2006). However, these studies focused on older adults, while habitual effects of physical activity on healthy middle-aged adults' cognitive function are poorly investigated. In addition, public health guidelines recommend regular physical activity throughout the lifespan, including for healthy adults of all ages (Garber et al., 2011; WHO, 2020). Few studies from Asia, including Japan, have investigated the relationship between physical activity and cognitive function by using step counts, objectively measured physical activity indices, including not only the older adults but also middle-aged and older adults.

Given this background, we examined the relationship between the average 7-day step counts and cognitive function in a community-based sample of middle-aged and older Japanese men aged 40–79 years.

2. Methods

2.1. Participants

The Shiga Epidemiological Study of Subclinical Atherosclerosis (SESSA) is a study on subclinical atherosclerosis and its determinants in a sample of Japanese residents. Details of the enrollment methods have been reported previously (Fujiyoshi et al., 2020; Kadota et al., 2013; Moniruzzaman et al., 2020; Ueshima et al., 2016). In brief, between 2006 and 2008, we randomly selected and invited 2,379 Japanese men aged 40–79 years, who were residents of Kusatsu City, Shiga, based on the Basic Residents' Register of the city, to participate in our study. Kusatsu city is located in central Japan and has an industrial structure similar to the average of Japan. Individuals with clinical cardiovascular disease, or other severe physical or mental diseases, potentially hindering their participation in physical activities, were excluded from the study. A total of 1,094 men agreed to participate in the baseline examination (participation rate: 46%). Step counts was measured during the baseline examination period (May 2006 to May 2008). Between 2009 and 2014, all participants were invited to participate in a follow-up examination, which included an assessment of cognitive function; 853 (78.0%) agreed. Cognitive function assessment was measured from June 2010 to August 2014 during the follow-up period (2009–2014). The mean follow-up period was 4.8 years. In this present study, using a priori criteria, we excluded participants whose consecutive 7-day step counts were unavailable, those who had unreliable daily step counts ($<$500 or $\geq$ 20,000) (n = 119), Cognitive Abilities Screening Instrument (CASI) was not administered (n = 34), history of stroke (n = 24), or missing other pertinent variables (n = 58), leaving 676 men for the final analyses. Written informed consent was obtained from all the participants. The study was approved by the Institutional Review Board of Shiga University of Medical Science (G2008-061).

2.2. Measurements

2.2.1. Measurement of step counts

Step counts were used to objectively measure SESSA participants at baseline (2006–2008) using a pedometer (DIGI-Walker, DW-200; Yamasa Tokei Keiki, Tokyo, Japan) for 7 consecutive days, including Saturday and Sunday. Before the measurements, participants were briefed on pedometer handling and is accurate measurement practices. Then, participants were asked to wear the pedometer constantly on the right anterior lumbar region of their waist belt except while sleeping, bathing, and performing other water activities for 7 consecutive days. Step count records were completed by the participants on a prescribed recording form for each day, along with the date of measurement, and mailed to the survey office after 7 consecutive days. We included only those participants who had complete step count data for 7 consecutive days without any outliers ($<$ 500 or $>$ 20,000 steps/day). We then calculated the 7-day average step counts used for all analyses in the current study.

2.2.2. Cognitive function

Cognitive function was assessed during follow-up examinations (2009–2014) using participants' performance on the CASI score (Version J-1.0). CASI is a validated and reliable instrument that is a comprehensive measure of intellectual and global cognitive function developed for use in cross-cultural and cross-national studies (Teng et al., 1994). Three raters (AF, NM, and YS) independently determined the CASI score based on recorded responses from participants. The CASI comprised of 25 questions in 9 domains (tasks measuring attention, concentration, orientation, short- and long-term memory, language, visual construction, list-generating fluency, and abstraction/judgment). The total CASI score ranges from 0 to 100, with higher scores indicating better cognitive function. For example, a CASI score of 82 corresponds to a score of 25–26 on the Folstein Mini-Mental State Examination (MMSE), and a score of 74 corresponds to a score of 22–23 on the MMSE, a level often used to indicate cognitive impairment (Abbott et al., 2004; Miyagawa et al., 2021). The intraclass correlation coefficient across the raters was 0.977 based on recorded samples of 20 participants.

2.2.3. Other factors

Data regarding medical history and other lifestyle factors were collected using a self-administered questionnaire. Lifestyle factors, including education (years), smoking and drinking status (current/past/never), use of medications for hypertension, diabetes, and dyslipidemia, and physical activity level during leisure time, were obtained from each participant using a self-administered questionnaire at baseline. Trained research staff members confirmed their responses to the completed questionnaire. Hypertension was defined as having an average systolic blood pressure $\geq$ 140 mmHg, or diastolic blood pressure $\geq$ 90 mmHg, or the use of medication for hypertension. Diabetes mellitus was defined as having a fasting blood glucose level $\geq$ 126 mg/dL or a concentration of glycated hemoglobin (HbA1c) value as converted by the National Glycohemoglobin Standardization Program $\geq$ 6.5% and/or the use of antidiabetic medication. The frequency of physical activity in leisure time was asked and categorized as "often," "occasional," or "rare or never.".

2.3. Statistical analysis

We calculated the participants' 7-day average step counts and divided them into quartiles. In the primary analysis, we used multivariable linear regression analyses to assess the association between the exposure "7-day average step counts" and the outcome of interest "cognitive function by CASI score," mainly into 4 models. We first computed the unadjusted and adjusted means of the CASI score, in accordance, with the quartiles of step counts using the analysis of covariance. P-values for trends were obtained with continuous CASI scores by treating the quartiles of step counts as ordinal. Second, we calculated the adjusted slope of the CASI score per 1,000 steps/day using linear regression. We also adjusted for the following covariates throughout the models: Model 1 included minimum adjustments for age (years) and education (years); Model 2 was additionally adjusted for smoking (current/past/never) and drinking (current/past/never); Model 3 was further adjusted for hypertension (yes/no), diabetes mellitus (yes/no), lipid medication (yes/no), and the body mass index (BMI) (kg/m^2). Statistical significance was set at $p < 0.05$, and all analyses were two-tailed. SAS version 9.4 software (SAS Institute, Cary, North Carolina, USA) was used for all statistical analyses.

3. Results

Of the 676 participants, the mean values for age, 7-day average step counts, and CASI score were 63.8 (standard deviation [SD], 9.1) years, 7,817 (2,984) steps, and 90.8 (5.8), respectively. There were 12 participants (1.8%) with CASI score of 74 or less, and 52 participants (7.5%) with CASI score of 82 or less. The participant characteristics for the overall and step count quartiles are presented in Table 1. The most common occupation of the participants at baseline was "employee, civil servant" (43.8%), followed by "none" (32.5%). The most common leisure-time physical activity was "occasional (46.6%)." The mean age, mean BMI and some other variables were statistically different among the step count quartiles.

Table 2 shows unadjusted and adjusted mean CASI scores according to the quartiles of step counts. Higher quartiles of average step counts were associated with higher CASI scores in a dose–response manner in all of the models. This trend was similar after adjusting for age, education, and other confounding factors, with a significant linear relationship between average step counts and CASI score (e.g., 89.8 – 91.3 from Q1 - Q4 in Model 2, p for trend = 0.008).

When average step counts were included in the models as a continuous variable, greater step counts were significantly associated with higher CASI scores independent of potential confounders (Table 3). An increment of 1,000 steps was significantly associated with a 0.21 higher CASI score, and this coefficient was approximately equivalent to a CASI slope of −0.23 for each additional year of age.

4. Discussion

We found a positive independent association between physical activity assessed by 7-day average step counts at baseline and the CASI score at follow-up in a community-based sample of middle-aged and older Japanese men. In this study, participants with higher 7-day average step counts were associated with higher CASI scores on an average 5 years later (at follow-up). This relationship was similar after adjusting for age and educational level. The relationships were also consistent in other models adjusted for smoking and drinking status and potential cardiovascular risk factors. Our results were in line with those of similar studies using average steps conducted in the older participants (Calamia et al., 2018; Chang, 2020; Rabin et al., 2019; Yoshiuchi et al.,

Table 2
Unadjusted and multivariable-adjusted mean CASI score according to the quartiles of step counts, 676 men, Shiga, Japan*.

Quartiles of average step counts per day	Unadjusted	Model 1	Model 2	Model 3
Q1	89.5 (88.6–90.4)	90.2 (89.4–91.0)	89.8 (88.9–90.7)	89.7 (88.7–90.6)
Q2	90.1 (89.3–91.0)	90.4 (89.6–91.2)	89.8 (88.9–90.8)	89.8 (88.8–90.8)
Q3	91.2 (90.3–92.1)	90.6 (89.8–91.4)	90.1 (89.1–91.1)	90.1 (89.1–91.0)
Q4	92.2 (91.3–93.1)	91.8 (91.1–92.6)	91.3 (90.3–92.3)	91.3 (90.3–92.2)
P for trend	<0.001	0.004	0.008	0.005

Abbreviations: CASI, Cognitive Abilities Screening Instrument.
Values are means (95% confidence interval).
P for trend was obtained by treating the quartiles as ordinal.
Model 1 was adjusted for age (years) and education (years).
Model 2 was further adjusted for smoking (current/past/never) and drinking (current/past/never).
Model 3 was further adjusted for hypertension (yes/no), diabetes mellitus (yes/no), lipid medication (yes/no), and body mass index (kg/m^2).
* Step counts and other factors were surveyed in 2006–2008, and CASI scores were surveyed in 2009–2014. The mean follow-up period was 4.8 years and the loss to follow up was 22%.

Table 1
Baseline characteristics according to the quartiles of step counts, 676 men aged 40–79 years, Shiga, Japan, 2006–2008.

	Total (N = 676)		Average step counts over 7 consecutive days (step/day) <5552 4134 (1032) Q1 (n = 169)		5553–7582 6685 (576) Q2 (n = 169)		7583–9774 8635 (581) Q3 (n = 169)		≥9775 11812 (1540) Q4 (n = 169)		*P**
Age, years	63.8	(9.1)	66.0	(10.0)	64.9	(8.4)	62.0	(9.3)	62.4	(8.1)	<0.001
Education, years	12.6	(2.9)	12.2	(3.3)	12.6	(2.7)	12.8	(2.8)	12.6	(3.0)	0.324
Body mass index, kg/m^2	23.6	(3.0)	24.5	(3.4)	23.6	(2.7)	23.4	(3.0)	23.1	(2.6)	<0.001
Systolic blood pressure, mmHg	135.5	(18.2)	136.3	(17.5)	137.2	(20.1)	134.4	(17.6)	133.9	(17.3)	0.279
Glucose, mg/dL	103.0	(20.7)	105.0	(22.1)	101.5	(19.2)	102.9	(19.7)	102.4	(21.6)	0.449
Hypertension, %	54.6		59.8		57.4		50.3		50.9		0.208
Diabetes mellitus, %	23.5		26.0		24.9		23.7		19.5		0.520
Lipid medication, %	14.4		21.3		14.8		10.7		10.7		0.015
Smoking, %											0.067
Current	32.3		35.5		38.5		32.5		22.5		
Past	50.2		48.5		43.8		50.9		57.4		
Never	17.6		16.0		17.8		16.6		20.1		
Drinking, %											0.006
Current	78.3		67.5		81.7		81.7		82.3		
Past	5.2		8.3		3.0		3.6		5.9		
Never	16.6		24.3		15.4		14.8		11.8		
Occupation, %											<0.001
Agriculture, forestry, and fishery	3.1		3.0		1.8		3.0		4.7		
Self-employed	11.2		11.8		14.8		9.5		8.9		
Employee, civil servant	43.8		30.2		37.3		52.1		55.6		
None	32.5		47.3		36.1		28.4		18.3		
Others	9.3		7.7		10.1		7.1		12.4		
Frequency of physical activity in leisure time, %											<0.001
Often	26.5		13.0		20.7		33.1		39.1		
Occasional	46.6		47.9		50.3		42.0		46.2		
Rare or never	26.9		39.1		29.0		24.9		14.8		

Values are means (standard deviations) unless otherwise specified.
**P*-values were calculated using one-way analysis of variance or chi-square tests.

Table 3
Multivariable adjusted slope of CASI score using linear regression analyses, 676 men, Shiga, Japan*.

	Slope of CASI score	95% CI	*P*
Step counts (per 1000 counts)	0.21	0.07 to 0.34	0.003
Age (per 1 year)	−0.23	−0.28 to −0.18	<0.001
Education (per 1 year)	0.48	0.34 to 0.61	<0.001
Body mass index (per 1 kg/m^2)	0.05	−0.09 to 0.19	0.465
Hypertension (yes)	−0.53	−1.35 to 0.30	0.211
Diabetes mellitus (yes)	−0.80	−1.72 to 0.13	0.091
Lipid medication (yes)	0.76	−0.36 to 1.89	0.184
Smoking (versus never)			
Current	−0.28	−1.43 to 0.87	0.634
Past	−0.13	−1.19 to 0.93	0.814
Drinking (versus never)			
Current	0.38	−0.66 to 1.42	0.469
Past	−1.35	−3.28 to 0.58	0.171

All variables are included simultaneously in the model.
* Step counts and other factors were surveyed in 2006–2008, and CASI scores were surveyed in 2009–2014.

2006), with only one study (Spartano et al., 2019) involving American adults including middle-aged participants. To the best of our knowledge, this study is among the first to examine the association between step count and cognitive function in Asians, including middle-aged community-dwelling men.

Most of the evidence on the association between physical activity, age-related neurodegeneration, and cognitive decline has relied on self-reported physical activity in older adults (Kishimoto et al., 2016; Willey et al., 2016). A few previous studies in middle-aged adults suggest that promoting an active lifestyle may reduce the risk of dementia later in life (Chang et al., 2010; Engeroff et al., 2018). However, their protective effects were inconsistent and inconclusive (Gross et al., 2017; Sabia et al., 2017). This may be due to the reliance on self-reported physical activity assessment. When given subjective analyses, participants typically find it difficult and complex to complete the questionnaire with a detailed response/recall of physical activity within a certain period. These results lead to discrepancies in physical activity measurement. Therefore, it is difficult to establish the reliability and validity of questionnaires (Washbum & Montoye, 1986). In addition, self-reported physical activity may be subject to reporting bias and recall bias (e.g., social desirability and inaccurate memory) and, thereby, measurement error. Step counts can potentially eliminate these limitations. Importantly, step counts are a fundamental unit of human locomotion and are thus a preferred metric for quantifying physical activity (Bassett et al., 2017). Pedometers are widely used to capture daily step counts at the population level and are easy to use in daily life with little discomfort to the user. A few previous studies on physical activity during the adult life span and cognitive function during old age have analyzed objectively measured physical activity using pedometers and accelerometry. Because step counts measure basic human behavior, there is biological variability, and to obtain valid and reliable estimates, steps should be measured within 7-days, including Sunday (Baumgart et al., 2015; Clemes et al., 2008). This study considered this issue and evaluated step counts on 7 consecutive days, including Saturday and Sunday.

The optimal duration of the activity, the type and intensity of the exercise, and the period during a person's lifespan are still not clear to maximize potential protective effects (Baumgart et al., 2015). The amount of physical activity recommended by guidelines in Western and Asian countries was estimated to be approximately 7,000 to 10,000 steps/day (Garber et al., 2011; Tudor-Locke et al., 2011). Still, it is unclear and debatable how much of an increase from the current level would be effective. The present study suggests that an increase of 1,000 average daily step counts may offset cognitive decline by approximately one year. The average step counts of the Japanese population measured at the same time as the baseline of the present study were reported to have decreased by nearly 1,000 steps per day compared to 10 years earlier and continued to decrease after that (Takamiya & Inoue, 2019). This finding may reflect the clinical importance of walking for preserving cognitive results in apparently healthy adults since daily steps decreased with age in men (Takamiya & Inoue, 2019). These may involve a lower cardiovascular risk profile (Inoue et al., 2012; Rabin et al., 2019), maintenance of hippocampal volume (Machida et al., 2022) and reduced loss of brain tissue (Chang et al., 2010; Rabin et al., 2019) due to increased daily steps. Recent studies by our colleagues on the same sample as the present study suggest that an increased number of daily steps plays an essential role in showing substantial clinical significance for brain atrophy (Moniruzzaman et al., 2021) and white matter lesions (Moniruzzaman et al., 2020).

For maximum impact, the social implementation of our research findings should be considered. Lifestyle-related preventive intervention strategies targeting societal increases in physical activity in midlife may help to delay or prevent dementia because there are no drugs to stop or reverse the dementia process (Iso-Markku et al., 2022). Simple and inexpensive pedometers can easily be adopted for clinical and real-world applications, including direct use by the general public as a tool for motivating physical activity (Tudor-Locke et al., 2011). Many wearable devices, such as smartphone applications and smart watches, have been developed recently to measure physical activity easily. It would be important for people to improve their physical activity by using these devices on a daily basis. Although not many adults meet the WHO guideline (WHO, 2020) recommendations for moderate-to-vigorous physical activity promotion (Macniven et al., 2012; Tucker et al., 2011), it is reasonable and feasible to capture physical activity in terms of step counts because the higher the daily step counts, the more significant the relative contribution of time spent in moderate-to-vigorous physical activity (Amagasa et al., 2021). In addition, pedometer usage per se may induce a Hawthorne effect of 20% or more (Bravata et al., 2007; Snyder et al., 2011), in which participants consciously increase their step counts. Therefore, it is important to have a step goal (Bravata et al., 2007) as per our results, in which steps increase by 1,000 step counts per day. We believe that the results of the present study will provide new insights into the health impacts of daily steps.

This study had some limitations. The first limitation was that cognitive function was not assessed at the baseline. Step counts were measured 5 years prior to the cognitive assessment. Thus, the likelihood of reverse causality for lower step counts resulting from potential cognitive decline is low. Second, data for the present study were only available for men; therefore, the findings cannot be adapted to women. Further research for the broader middle-aged and older adult population, including women, are needed to assess the generalizability of these results. Third, pedometers cannot capture some types of physical activity, such as swimming, cycling, and weightlifting. In addition, 7-day step count assessed by the pedometer in this study may not accurately evaluate the participants' overall physical activity level. It would be underestimated. Finally, other unmeasured factors affecting both physical activity and cognitive function may have led to residual confounding.

5. Conclusions

Our results showed that a greater 7-day average step count at baseline was associated with significantly higher cognitive function 5 years later at follow-up in apparently healthy middle-aged and older Japanese men. These findings suggest that a higher number of steps is associated with better cognitive function.

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CRediT authorship contribution statement

Takeshi Shibukawa: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. **Akira Fujiyoshi:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Project administration, Writing – review & editing. **Mohammad Moniruzzaman:** Writing – review & editing. **Naoko Miyagawa:** Data curation. **Aya Kadota:** Data curation. **Keiko Kondo:** Data curation. **Yoshino Saito:** Data curation. **Sayaka Kadowaki:** Data curation. **Takashi Hisamatsu:** Data curation, Writing – review & editing. **Yuichiro Yano:** Supervision. **Hisatomi Arima:** Supervision, Writing – review & editing. **Ikuo Tooyama:** Supervision. **Hirotsugu Ueshima:** Funding acquisition, Project administration, Writing – review & editing. **Katsuyuki Miura:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Project administration, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Akira Fujiyoshi reports financial support was provided by Japan Society for the Promotion of Science. Hirotsugu Ueshima reports financial support was provided by Japan Society for the Promotion of Science. Katsuyuki Miura reports financial support was provided by Japan Society for the Promotion of Science. Hirotsugu Ueshima reports financial support was provided by Glaxo-Smith Kline GB.

Data availability

Data will be made available on request.

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Appendices

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