Tri-axial accelerometer-determined daily physical activity and sedentary behavior and functional capacity in community-dwelling Japanese older adults

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Summary

Considerable evidence shows that higher levels of physical activity (PA) in late life are associated with reduced risks of several chronic diseases, better physical and mental health, as well as lower rate of all-cause mortality. In contrast, sedentary behavior (SED), such as sitting or reclining in free-living daily condition, has recently emerged as a new public health risk, independent of PA levels. To date, most of the evidence has primarily relied on subjective measurements of these behaviors, which are prone to a variety of biases, particularly in older adults. Studies with more accurate assessment of the daily levels of PA and SED, such as accelerometer, are needed for better understanding the current population levels of PA and SED, and quantifying the does-response relationships with health outcomes in older adults. Therefore, the doctoral thesis had the following two objectives: (1) to objectively assess daily PA and SED in community-dwelling older adults, using tri-axial accelerometers; (2) to evaluate the associations between these objectively measured PA and SED and selected health conditions such as functional disability and cognitive function in community-dwelling older adults.
Tri-axial accelerometer-determined daily physical and sedentary behavior of suburban community-dwelling older Japanese adults (Study I)

Participants of this study were from the baseline survey of the Sasaguri Genkimon Study (SGS-1), who were 65 years or older and not certified as those requiring long-term care. Levels of PA and SED were assessed objectively for seven consecutive days using tri-axial accelerometer. A total of 1,739 participants (median age: 72 years, men: 38.0%) with valid accelerometer data were included. Overall, participants in the present study spent 54.5% of their waking time being sedentary, and only 5.4% was moderate-to-vigorous physical activity (MVPA). Women accumulated more minutes of light physical activity (LPA) and MVPA compared with men. In contrast, men spent more time being sedentary. Mean steps per day did not differ between sexes. Furthermore, participants with higher body mass index (BMI ≥25) had lower PA levels, and longer SED compared with those with lower BMI (BMI <25). PA levels were lower and SED was longer with age. The present study is the first to demonstrate that the levels of PA and SED differed by sex, age, and BMI in Japanese community-dwelling older adults. The findings also showed a high level of SED and low level of PA in the Japanese older population. Data presented in the study will enable further investigation of additional determinants of PA and SED in order to develop effective
population-based intervention strategies to promote PA and reduce prolonged SED in the Japanese population and possibly other rapidly aging societies.

**Associations of tri-axial accelerometer determined sedentary time and breaks in sedentary time with disability in instrumental activities of daily living in community-dwelling older adults (Study 2)**

Study 2 was performed to examine cross-sectional associations of objectively measured sedentary time (ST) and breaks in sedentary time (BST) with instrumental activities of daily living (IADL) disability. As in Study 1, participants of this study were from the SGS-1. SED (such as ST and BST) and PA were measured using a tri-axial accelerometer. BST was defined as at least 1 minute where the intensity of activity rose up to or above 1.5 metabolic equivalents (METs) following a sedentary bout. Disability was defined as inability in at least one of IADL tasks using the Tokyo Metropolitan Institute of Gerontology Index of Competence. After adjusting for potential confounders and MVPA, longer ST was significantly associated with higher likelihood of IADL disability, whereas greater number of BST was associated with lower likelihood of IADL disability. ST and BST remained statistically significant after mutual adjustment with odds ratio of 1.30 [95% confidence interval (CI): 1.00-1.70] and 0.80 (95% CI, 0.65-0.99), respectively. After adjusting for confounders and ST, there were no
significant association between MVPA and IADL disability. This study first demonstrated that shorter ST and higher number of BST were associated with lower risk of IADL disability independent of MVPA, and that the association for ST was independent of BST, and vice versa. These findings suggest not only total ST but also the manner in which it is accumulated may contribute to the maintenance of functional independence in older adults.

**Association between tri-axial accelerometer-determined daily physical activity and cognitive function: a longitudinal population-based cohort study (Study 3)**

Participants for this study were individuals who had participated in both baseline (SGS-1) and the first follow-up phrase of Sasaguri Genkimon Study (SGS-2). A total of 672 community-dwelling older adults (mean age: 72.3 years, male: 39.9%) without dementia at baseline were involved in this study. Total PA including LPA and MVPA was measured by a tri-axial accelerometer. Cognitive function was assessed by the Japanese version of Montreal Cognitive Assessment (MoCA-J). In the multiple regression model, total physical activity was not associated with the follow-up MoCA-J score (regression coefficient: -0.04; 95% CI: -0.10 to 0.01; p=0.12), after adjusting for socio-demographic and lifestyle factors, as well as physical function, distress, depression, vascular-related diseases and baseline MoCA-J score. There was no linear
relationship between objective measured total PA and follow-up cognitive function over 2 years in this cohort. Findings in the present study indicated a longer follow-up period might be needed to assess the relationship between physical activity and normal cognitive aging.

In conclusion, this doctoral thesis reveals that Japanese older adults spent majority of the day being sedentary and accumulated few minutes of MVPA, and confirms that SED is a distinct concept from insufficient MVPA and has independent effects on health outcomes in older adults. These findings highlights the need of reducing overall time spent in SED in community-dwelling older adults to optimize their health, beyond encouraging PA. In addition, it also suggests breaking up prolonged sedentary time may be beneficial for the maintenance of functional capacity in older adults. Although no significant association between accelerometer-determined PA and cognitive function was observed, the doctoral thesis has shown the feasibility and utility of the accelerometer in longitudinal, large-scale epidemiology studies. Further studies will be performed investigate the associations of these objectively measured behaviors with other health conditions and the incidence of hard clinical endpoints (e.g., dementia, all-cause mortality) to facilitate development of guidelines related to PA and SED in this population.
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Abbreviations

95% CI: 95% confidence interval

ANOVA: analysis of variance

BADL: basic activity of daily living

BMI: body mass index

BST: breaks in sedentary time

DLW: doubly labeled water

HR: hazard ratio

IADL: instrumental activities of daily

IQR: interquartile range

K6: Kessler 6 psychological distress scale

LPA: light physical activity

METs: metabolic equivalents

MMSE: Mini-Mental State Examination

MoCA-J: Japanese version of the Montreal Cognitive Assessment

MVPA: moderate-vigorous physical activity
NHANES: National Health and Nutritional Examination Survey

OR: odds ratio

PA: physical activity

PAEE: physical activity energy expenditure

RMR: resting metabolic rate

SD: standard deviation

SED: sedentary behavior

SGS: Sasaguri Genkimon Study

SGS-1: baseline of Sasaguri Genkimon Study

SGS-2: first follow-up phrase of Sasaguri Genkimon Study

ST: sedentary time

TMIG-IC: Tokyo Metropolitan Institute of Gerontology Index of Competence
Chapter 1. Background and purpose of the doctoral thesis
1. Background

A large body of epidemiological evidence, accumulated over the past few decades, has demonstrated the extensive health benefits of physical activity (PA) throughout the life span. As noted in the Global Recommendations on PA for health, the health benefits include decreased mortality rates and lower risk of various non-communicable diseases, including hypertension, cardiovascular disease, stroke, type 2 diabetes mellitus, colon cancer and breast cancer (World Health Organization, 2010). There is also evidence that PA delays the progression of functional limitation (Paterson and Warburton, 2010) and cognitive impairment (Morgan et al., 2012), and reduces the risk of disability (Keysor et al., 2003) and dementia (Blondell et al., 2014; Morgan et al., 2012) in older adults. Indeed, physical inactivity has been estimated as the fourth leading risk factor for mortality and major risk factor for non-communicable diseases in the world (World Health Organization, 2010). In contrast, sedentary behavior (SED), such as sitting or reclining in free-living daily condition, is increasingly recognized as a distinct risk factor from too little PA for deleterious health outcomes such as cardiovascular disease (Chomistek et al., 2013), type 2 diabetes mellitus (Biswas et al., 2015) and mortality (Koster et al., 2012). Therefore, public health strategies targeted increasing PA and reducing SED in daily life are needed to optimize the health in older adults.
To evaluate the efficacy of intervention strategies aiming to increase PA and decrease SED, it is important to measure activity levels accurately within the population studied. Furthermore, accurate measurement of PA and SED levels is vital to improve the understanding PA and SED levels within the general population as well as to quantify the dose-response relationships between activities and health outcomes. However, knowledge regarding population level of PA and SED is scarce in Japan. Current available data is primarily based on subjective methods, which are prone to a variety of biases, particularly in older adults.

Recently, accelerometer-based methods have been widely accepted as more accurate and objective measures of PA and SED in a number of populations including older adults (Lee and Shiroma, 2014; Murphy, 2009), which might provide insight into these daily behaviors in older adults. The focus of this thesis is therefore to explore the accelerometer-determined PA and SED levels in community-dwelling older Japanese adults and investigate their associations with some health conditions such as disability and cognitive function.

This chapter firstly provides definitions of the terms “PA” and “SED”, followed by a brief overview of the most commonly used methods for assessing PA and SED. Subsequently, current data regarding large-scale accelerometer-determined levels of PA
and SED is described. Finally, existing literature on the associations between PA and SED and health outcomes, with a special focus on disability and cognitive function, is discussed.

2. Physical activity and sedentary behavior definitions

PA is defined as “any bodily movement produced by skeletal muscles that results in energy expenditure” (Caspersen, et al., 1985). PA is a complex behavior and is commonly quantified by the following four dimensions 1) frequency: the number of sessions of days per week or month an activity performed; 2) duration: the time spent in one bout of an activity; 3) intensity: the level of effort required to perform a specific activity and often expressed in terms of metabolic equivalents (METs); 4) type of activity. PA is commonly quantified by quantifying how much time a person spends in different PA intensity categories [e.g., light PA or LPA (1.6 METs-2.9METs) and moderate-vigorous PA or MVPA (≥3 METs)].

At the other hand, SED is defined as “any waking behavior characterized by an energy expenditure ≤1.5 METs while in a sitting or reclining posture” (Pete et al., 2008). Emerging evidence suggests that SED is a distinct concept from insufficient PA and has independent effects on health outcomes (Tremblay et al., 2010). In this context, an
individual may be described as sedentary if they engage in a large amount of SED, while physical inactivity is used to describe those who are not meet specified PA recommendations (Tremblay et al., 2010).

3. Assessments

The methods of assessing free-living PA can be generally summarized as 1) subjective measure such as questionnaires, diaries, logs, recalls; 2) objective measures such as accelerometers, pedometers, heart rate monitoring, and doubly labeled water (DLW) method. In the following, the most commonly used measures for PA and SED are briefly presented with an emphasis on accelerometer, as it is the method used in this thesis.

3-1. Subjective method

Self-report questionnaires are the most commonly used to estimate levels of PA and SED for reasons of low cost and feasibility in large-scale population-based studies. Besides, many questionnaires are able to capture valuable information by characterizing PA by frequency, intensity, duration, and type (Welk, 2002), and measuring domains of SED (e.g., context, duration) (Atkin, et al., 2012). However, activity information obtained by such self-report measures is subject to several potential response biases.
(e.g., social desirability, imprecise recall, misinterpretation) (Craig et al., 2003). In older adults in particular, self-report questionnaires may also be influenced by health status, disturbances to memory and cognition, and fluctuations in mood, anxiety, and depression (Shephard, 2003; Rikli, 2000). Moreover, older adults often irregularly engage in light activities as part of daily life activities more frequently than MVPA, which makes it difficult to recall (Golubic et al., 2014). Finally, many of the existing subjective tools fail to measure SED and light PA adequately (Shephard, 2003). Therefore, objective measures of PA and SED are needed to increase knowledge regarding the daily levels of PA and SED and their roles for health in older adults.

3-2. Objective method

To address some of the limitations related to subjective methods, objective measures of PA such as accelerometer and pedometers are becoming more commonly used methods in population-based studies. In the following, objective measures including DLW, heart rate monitors, pedometers and accelerometers are presented.

3-2-1. The doubly labeled water (DLW) method

The DLW is considered the gold standard to determine free-living energy expenditure over a given period of time. Combined with measurement of the resting metabolic rate (RMR), PA energy expenditure (PAEE) can be calculated (Manini et al., 2006; Schoeller
et al., 1986). However, this method can only provide total PAEE and little information regarding patterns of PA in terms of frequency, duration, intensity or type. In addition, DLW is not feasible for use in large population studies because of high cost.

3-2-2. Heart rate monitoring

Heart rate monitoring has been used to estimate PAEE based on the assumption of a linear relationship between heart rate and oxygen consumption in activities of MVPA (Wilmore and Haskell, 1971). Because the relationship between heart rate and oxygen consumption is unique to each individual and is somewhat attenuated during low and high intensity activities, individual calibration curves are necessary for estimation of PAEE (McCorry et al., 1997). Therefore, this technique is easy to administer in a laboratory setting, but may become burdensome in a large sample size. In addition, heart rate can be affected by several factors other than PA, such as emotion and environmental factors (ambient temperature and humidity) (Lee, 2009).

3-2-3. Pedometers

Pedometers are small, inexpensive and simple devices that have the ability to quantify ambulation in terms of accumulated number of steps during walking or running. However, pedometers may underestimate steps taken in individuals at slower gait speeds (Crouter et al., 2003; Le Masurier, et al., 2004) or with irregular gait patterns
(Cyarto et al., 2004), which may limit their use in older population. Although newer generations of pedometer have been developed to improve sensitive for slower walking speeds and have been recommended for use in older adults (Crouter et al., 2005; Melanson et al., 2004), pedometers are limited to assessing ambulatory activity only. Time spent in intensity-specific activities cannot be assessed using the pedometer, which could be an important limitation where the relationship between PA and a health outcome is intensity dependent.

3-2-4. Accelerometers

Accelerometers are small battery-operated devices commonly worn on the waist that measure accelerations of the body movements in single or multiple planes (vertical, medio-lateral, and antero-posterior) (Chen et al., 2005). Many of the accelerometers are now capable of recording and storing data (e.g., acceleration counts per minute) over long periods of time and these data can later be easily downloaded to a computer (Chen et al., 2005).

To translate accelerometer data (e.g., counts per minute) into estimate of energy expenditure or time spent in various intensity categories, previous calibration studies have used a single linear regression to obtain prediction equations that calibrate the activity counts from the vertical axis only to estimate PAEE or METs and designated
activity count cut-points corresponding to specific-intensity activities have been extensively used to distinguish intensity categories (e.g., SED, LPA and MVPA) (Freedson et al., 1998; Hendelman et al., 2000; Swartz et al., 2000). However, most of the equations have derived only from locomotive activities, which was found to significantly underestimate the intensity of most lifestyle activities (e.g., laundry, washing dishes, cooking, vacuuming, and gardening) (Bassett et al., 2000; Hendelman et al., 2000), whereas, the equations developed on moderate-intensity lifestyle activities tended to overestimate sedentary and light activities (Crouter et al., 2006). It may therefore be inappropriate to apply these single regression equations developed using either locomotion or moderate-intensity lifestyle activities to free-living conditions in attempts to determine PAEE or to classify PA intensity categories from sedentary to vigorous.

It has recently been shown that prediction models that account for the type of activity performed could result in more accurate estimation of PA intensity. For example, Crouter et al. (2006, 2010) has developed two-regression equation models of discriminating between locomotive activities (e.g., walking and running) and lifestyle activities based on the variability in the activity counts with a uni-axial accelerometer, providing a closer estimate than previous single regression models.
Newer accelerometer models including the device used in this thesis have become available for collecting acceleration data from all three axes (anterior-posterior, mediolateral, and vertical direction), which appear to provide a better predictions than uni-axial accelerometers (Plasqui et al., 2005). Indeed, some attempts have been made with a tri-axial accelerometer to improve estimates of intensity by defining a specific regression equation for classifying groups of activities such as locomotive, lifestyle, or sedentary activities (Bonomi et al., 2009; Oshima et al., 2010). The sensitivity and specificity for different type of activities ranges from 93% to 99%. For example, Bonomi et al. (2009) reported a classification accuracy of 93% across 20 selected activities (e.g., lying, sitting, walking and running) with a tri-axial accelerometer mounted on the lower back. For the tri-axial accelerometer used in this thesis, Oshima et al. (2010) had developed a simple algorithm based on the ratio of unfiltered to filtered acceleration that was able to distinguish between locomotive and non-locomotive activities with an accuracy of 98.7%. More recently, Ohkawara et al. (2011) showed that, using the classification algorithm with a triaxial accelerometer, clearly improved the accuracy of estimating the intensity of various PA and time spent in SED.

With the rapid development in technology and improvement in data reduction, accelerometers have allowed for more accurate and ‘real-time’ measurements of PA and
SED. However, it is important to note that accelerometers are not without limitations. For example, accelerometer is unable to truly capture the type of activity and provide information of the social and environmental context in which the activity occurs. Other limitations include the inability to assess certain type of PA (e.g., water activities, cycling, or resistance exercise) and distinguish between postures (e.g., sitting or standing). Given that walking is the most common PA and time spent in lower levels of activity over long periods likely indicate sitting rather than standing with little movement in older adults, these might not be the major limitations for elderly population (Lee and Shiroma, 2014).

As mentioned above, there are both advantages and limitations of the subjective and objective measures. To select an optimal assessment tool, it is important to consider targeted population characteristics such as age, gender, culture, and general health status (Pettee Gabriel et al., 2012). For example, older adults are generally the most sedentary and are more likely to engage in LPA, which may occur in irregular patterns and therefore are hard to capture by subjective measures (e.g., questionnaires). Furthermore, older adults might be also influenced by health status (e.g., cognition impairment) as mentioned before. Therefore, objective measures such as accelerometer may be preferable over the subjective methods in older populations. Besides, new data
processing techniques regarding accelerometers are emerging, such as pattern recognition or automatic identification models to identify specific activities carried out (Bastian et al., 2015; Crouter et al., 2006; Crouter et al., 2010; Ohkawara et al., 2011; Oshima et al., 2010). There is also an interest to detect changes in postural allocation (e.g., sitting, standing or transitions between these postures) with an accelerometer (Bassett et al., 2014). These advances in accelerometers would therefore allow for a better characterizing and classifying PA and SED in the assessment (Kumagai et al., 2015).

4 Accelerometer-determined population levels of physical activity and sedentary behavior

In recent years, accelerometers have increasingly been used to provide objective assessments of PA and SED in older population monitoring due to their convenience, assessment of multiple dimensions of PA (e.g., intensity, duration and frequency) and eliminating many of the limitations of subjective measures. However, most studies were carried out with relatively small sample size. There are few large-scale population-based studies that have assessed PA and SED using accelerometers in older adults, which are presented in the following.
Baptista et al. (2012) presented data on accelerometer (ActiGraph GT1M model; Fort Walton Beach, FL) measured PA and SED in representative sample of Portuguese population. A total of 4,649 participants were included in this study, and 679 out of them were older adults aged 65 years or older. Findings showed that the overall PA levels remained relatively stable with age until 50 years old, with a slight decline after reaching 50 years, and a steep decline after reaching 65 years. At the other hand, older adults aged 65 years or older were the most sedentary group in the population. The 2003-2004 National Health and Nutritional Examination Survey (NHANES) reported similar findings (Troiano et al., 2008). Results showed that older adults aged 60+ years were the most inactivity group in the U.S population. When combing NHANES data from 2003-2004 to 2005-2006, regardless the cut point of MVPA (e.g., 500 counts/minute or 2,000 counts/minute) used, time spent in MVPA was lower with each successive age group (60-69, 70-79, and ≥80), while time spent in SED was longer among participants aged 80+ as compared to younger groups of older adults (Evenson et al., 2012).

Another population-based study from Norway measured PA and SED by accelerometer (ActiGraph GT1M model, LLC, Pensacola, FL) in persons aged 65 years or older for 7 days (Lohne-Seiler et al., 2014). A total of 580 participants had valid
assessment. Total PA levels (counts per minute) and MVPA reduced as age increased, while time spent in SED increased. Overall, the Norwegian older adults spent 66% of their waking time in SED (9.3 hours), 24% in low-intensity PA (3.3 hours), 7% in lifestyle PA (1 hour) and 3% MVPA (30 minutes). In addition, Norwegian older men accumulated more minutes of MVPA per day compared to women, whereas women spent less time being sedentary and more time in low-intensity. Regarding the age and sex differences, similar findings also observed among other population-based studies among older adults in Iceland (Arnardottir et al., 2013), Canada (Colley et al., 2011), and United Kingdom (Davis et al., 2011).

Indeed, there are several studies assessed PA levels by accelerometers (Kenz Lifecorder, Suzuken, Nagoya, Japan) in Japanese older adults. For example, one study (n=802) of older adults recruited from six cities in Japan reported that the mean (standard deviation or SD) of time spent in LPA (defined as 1.8-2.9 METs) and MVPA (defined as ≥3.6 METs) were 57.1 (22.7) and 17.6 (15.3) minutes per day (Osuka et al., 2015). The Nakanojo study assessed PA levels among 170 older adults aged 65-84 years over one year (Aoyagi et al., 2009). The total sample spent 17.3 minutes in at least moderate PA (defined as >3.0 METs) and accumulated 6,574 steps per day. Year-averaged number of steps taken and time spent in at least moderate PA per day.
were higher in men than women, which are in accordance with the western population mentioned above.

Although findings from the above studies provide objectively measured PA and SED with accelerometers, the variety in used accelerometer and data reduction methods make the direct comparison of these different surveys into a challenging enterprise. For example, within the nine studies mentioned above, six different accelerometer models, the Actigraph model 7416 (Evenson et al., 2012; Troiano et al., 2008), ActiGraph GT1M model (Baptista et al., 2012; Davis et al., 2011, Lohne-Seiler et al., 2014), ActiGraph model GT3X (Arnardottir et al., 2013), Actical (Colley et al., 2011), and Kenz Lifecoder (Aoyagi et al., 2009; Osuka et al., 2015) were used to assessed activities. There is some evidence that significant differences exist between the newer ActiGraph generations (GT1M and GT3X) and the model 7146 (Ried-Larsen et al., 2012), which may result in differences in mean PA level and across activity intensities (e.g., SED, LPA, and MVPA). As noted earlier, activity count cut-points method is the most commonly used to identify intensity-specific activities. However, there is no consensus about the cut-points to use to define PA intensity in older adults (Strath et al., 2012). For example, three cut-points were used for classifying MVPA, ranging from 500 to 2,020 counts per minutes in these eight studies, which would also result in a correspondingly
large range of minutes of MVPA. Therefore, care should be taken when retrospectively measuring intensity of activity or comparing data between studies (Kumagai et al. 2015). Nevertheless, given the findings from the above studies, older adults spend majority of their waking time being sedentary while they accumulate a few minutes of MVPA.

5. Associations of physical activity and sedentary behavior with disability

With the population aging and increased life expectancy worldwide, a rapid increase in the number of disabled elderly individuals places a large burden on public health and social security systems (Colombo et al., 2011; Fried et al., 2001). Identifying factors for preventing or postponing functional disability is therefore a critical issue for rapidly aging societies, such as Japan.

Many studies have investigated the relationship between PA and disability among older adults, and there have been systematic reviews that highlight the protective effect of PA on disability (Keysor, 2003; Paterson et al., 2010; Stuck et al., 1999; Tak et al., 2013). For example, a systematic review focused on the relationship between PA and outcomes of functional limitations, disability, or loss of independence among healthy community-dwelling older adults (Paterson et al., 2010). Although heterogeneity in the PA categorizations and in the outcome measures was present in reviewing this evidence,
consistent findings were shown for PA and disability. In general, higher PA, described as “moderate” or “vigorous” intensity activities, predicted higher functional status and was associated with lower risk of disability, while only one study suggested a significant effect for a light or low PA group (Østbye et al., 2002). However, the diversity in used definitions and methods to measure PA as well as disability precluded pooling the study results.

A recent systematic review has been carried out to present a meta-analysis of the association between PA and both incidence and progression of basic activity of daily living (BADL) disability in older community-dwelling adults (Tak et al., 2013). Among 373 papers reviewed, the authors identified 13 studies that reported prospective, longitudinal data on the association between PA and subsequent disability among community-dwelling adults, while nine studies reported incident disability and four studies reported on the progression of disability. The authors classified the level of PA as low, medium or high. According to the systematic review, a higher PA level (medium/high) was found to be associated with a decreased risk of incident BADL disability with odds ratio of 0.51 [95% confidence interval (CI): 0.38-0.68, p<0.001] based on the nine longitudinal studies. In additional, a higher PA level (medium/high) also reduced the risk of progression of BADL disability by 0.55 (95%CI: 0.42-0.71,
The authors also noted that the selected studies used a variety of ways to measure and categorize PA levels, where PA was usually measured with subjective measurement (e.g., a single question or a questionnaire).

Recent studies have evaluated the association of disability and objectively measured PA as well as SED using accelerometers. One research from the Rush Memory and Aging Project examined the association between total daily PA, measured by accelerometers (Actical, Mini Mitter, Bend, OR), and the BADL disability (Shah et al., 2012). Results showed that greater total PA was not only cross-sectionally associated with lower risk of BADL disability (OR per 105 counts/day increment: 0.55, 95% CI: 0.47-0.65) but also related with reduced hazard of developing disability by 25% (hazard ratio (HR): 0.75, 95% CI: 0.66-0.84) over a mean follow-up of 3.4 years. Another study by Cawthon et al. (2013) utilizing data from the Osteoporotic Fractures in Men, examined the association of objectively assessed total energy expenditure, time spent in MVPA and SED with the development of functional disabilities in 1,983 older men (aged ≥78.3) over 2 years. Energy expenditure and activity levels were measure using multisensory monitor (SenseWear Pro Armband, Body Media, Inc., Pittsburgh, PA). Functional disability was defined by inability to perform instrumental activities of daily living (IADL) or BADL. Results from this study showed that each standard deviation
(SD) decrease in total energy expenditure (420.6 kcal/day) increased the likelihood of IADL disability (odds ratio or OR: 1.61, 95% CI: 1.30–2.00) or BADL disability (OR: 1.35, 95% CI: 1.12–1.63). Each SD decrease in MVPA (61.1 minutes/day) increased the likelihood of IADL disability (OR: 1.47, 95% CI: 1.22–1.78) or BADL disability (OR: 1.36, 95% CI: 1.14–1.61). In addition, each SD increase in minutes of SED (105.2 minutes/day) increased the likelihood of IADL disability (OR: 1.20, 95% CI: 1.03–1.40) or BADL disability (OR: 1.17, 95% CI: 1.01–1.35).

More recently, a cross-sectional study using the data from the 2003-2005 NHANES examined the association between time spent in SED and disability in BADL (Dunlop et al., 2015). In this study, results showed a strong relationship between greater time spent in SED and the presence of BADL disability (OR per one hour/day increment: 1.46, 95% CI: 1.07-1.98). Importantly, the association between objectively measured SED and BADL is independent of MVPA indicating that SED is a distinct disability risk factor as opposed to insufficient MVPA or physical inactivity. In contrast, Marques et al. (2014) studied a group of Caucasian Portuguese older adults aged 65-74 years to examine the cross-sectional relationships of accelerometer-determined PA and SED (ActiGraph GT1M model; Fort Walton Beach, FL) with the risk of losing physical independence and found that SED was not significant associated with the risk of losing
physical independence after controlling for PA intensities (although higher levels of LPA and MVPA were found to decrease the risk of losing physical independence). Furthermore, results from the Cooperative Health Research in the Region of Augsburg study showed that the PA (LPA and MVPA) and SED measured by accelerometers (ActiGraph GT3X model, Pensacola, FL, USA)) were no longer related to the risk of disability (defined by the Health Assessment Questionnaire Disability Index) after controlling for sociodemographic and health factors (Orlieb et al., 2014). Although the negative data are important, limitations of these should be noted and discussed. For example, both studies used relatively small sample size (n<400) which may not reflect that of the general population. In addition, the first study was solely based on sample of Caucasian Portuguese population (Marques et al., 2014). These conflicting findings highlight the necessity for clarifying the role of accelerometer-determined intensity-specific PA and SED on disability in regions of different cultures and environments, such as Japan, with large-scale sample.

Given the above results and the facts that most of these studies have used subjectively measured PA data, little is known about the “dose-response” relationships between key PA indices or SED and disability. Larger studies with objectively measured activity are still required to confirm whether SED is a distinct concept from insufficient MVPA, or
whether SED has independent effects on health outcomes, such as disability.

6. Associations of physical activity and sedentary behavior with cognitive function

With many societies experiencing increasing longevity worldwide, age-related cognitive decline is another major public health concern. According to the Alzheimer’s Disease International, the number of people living with dementia worldwide in 2014 is estimated at 44 million, and will double by 2030 and more than triple by 2050 (Alzheimer’s Disease International, 2014). In Japan alone, 4.62 million people aged 65 or older have dementia in 2012, accounting for approximately 15% of the total older population (Asada et al., 2013). Given this epidemic scale and limited effective pharmaceutical treatments, identifying modifiable risk or protective factors for maintaining cognition or reducing the risk of dementia in the elderly are in urgent need.

A rapidly growing literature suggests that PA may attenuate cognitive impairment and reduce dementia risk (Bherer et al., 2013; Blondell et al., 2014; Brown et al., 2013; Carvalho et al., 2014; Hamer and Chida, 2008; Plassman et al., 2010; Sofi et al., 2010), although results from prospective studies have shown conflicting results. For example, Sofi et al. (2010) conducted a systematic review and meta-analysis of 15 prospective studies (12 cohorts) to assess the relationship between PA and the risk of cognitive
decline in non-demented individuals. Despite individual variation between studies (e.g., definitions of cognitive decline or PA levels), both low-to-moderate PA level (hazard ratio or HR: 0.65, 95% CI: 0.57-0.75, p<0.00001) and high PA level (HR 0.62, 95% CI 0.54-0.70; p<0.00001) resulted in a reduced risk of cognitive decline after follow-up periods ranging from 1-12 years. Another meta-analysis conducted by Hamer and Chida (2008) explored the role of PA on the occurrence of neurodegenerative diseases in non-demented individuals. Sixteen prospective studies were included in the overall analysis, which incorporated 163,797 non-demented participants at baseline with 3,219 cases of neurodegenerative disease at follow-up. In the overall analysis, the relative risk of overall dementia in the highest PA groups compared with the lowest or control groups was 0.72 (95% CI: 0.60–0.86, p<0.001), for Alzheimer’s disease 0.55 (95% CI: 0.36–0.84, p=0.006).

More recently, Blondell et al. (2014) conducted a systemic review to explore the associations of PA with cognitive decline and dementia in view of additional original research in the field, including a number of studies that used objective measures of PA. Twenty-one cohorts on PA and cognitive decline and twenty-six cohorts on PA and dementia were included in the meta-analysis. The relative risk for dementia and AD were lower in those with the higher level of PA suggesting a protective effect of high
levels of PA that reduces the risk of cognitive decline by 35% (95% CI: 0.55-0.76) and dementia by 24% (95% CI: 0.76-0.97).

Several studies have also been conducted to examine the association between SED and cognitive function. One such study by Kesse-Guyot et al. (2012) utilizing data from the SUpple´mentation en VItamines et Mine´raux AntioXydants examined the association between several types of SED (e.g., TV viewing and computer use) and cognitive function. Their cross-sectional findings showed that more time spent in using the computer was associated with a better performance in different cognitive domain (e.g., verbal memory and executive functioning), whereas time spent in TV viewing was negatively associated both performance on bother verbal memory and executive functioning. In addition, increase in time spent using the computer was associated with better cognitive function over a follow-up of 6 years. The association between TV viewing and executive functioning did not persist in the longitudinal analysis. In a separate prospective study, Hamer and Stamatakis (2014) observed that use of the internet as baseline was associated with higher global cognitive function at follow up. Furthermore, results from this study also showed negative longitudinal association between TV viewing and cognitive function. Results from these two studies indicate that the environmental and social contexts in which SED occur is important when
investigating the cognitive effects of SED.

Taken together, the findings presented above provide consistent and compelling evidence for the protective effect of PA on cognitive health, while limited evidence shows a negative association between passive SED and cognitive performance. As the studies focused on the relationships between PA, SED and disability, it should be noted that the cognitive assessment tools and the methods for measuring levels of PA and SED varied substantially across studies. With regard to PA, data were mostly obtained from subjective method (e.g., questionnaires), which may introduce various biases and often fail to provide sufficient information on the specific dose of PA, in terms of duration or intensity, which can prevent or delay cognitive decline and dementia. In addition, methods used to classify the level of activity varied across studies, ranging from a simple differentiation of active/not active to three or four levels of intensity, making it difficult to synthesize the findings. Further research with more sophisticated methods (such as accelerometers) in measuring and categorizing PA is needed to provide a clear evidence on what constitutes high levels of PA or whether there is a minimal threshold (e.g., duration or intensity) of PA for a reduction in risk of cognitive decline and dementia in older adults.
7. Purpose of the doctoral thesis

Given the above background, the primary purpose of this doctoral thesis was to assess daily PA and SED levels in community-dwelling Japanese older adults, and to investigate their associations with disability and cognitive function, using tri-axial accelerometers. Accordingly, the present thesis had three objectives. The first objective was to assess daily PA and SED in community-dwelling older adults, using tri-axial accelerometers (Study 1 in Chapter 2). The second objective was to examine the association between accelerometer-determined SED and IADL disability in community-dwelling older adults (Study 2 in Chapter 3). The third objective was to examine the association of accelerometer-determined PA and cognitive function in community-dwelling older adults (Study 3 in Chapter 4).
Chapter 2. Tri-axial accelerometer-determined daily physical activity and sedentary behavior of suburban community-dwelling older Japanese adults (Study 1)
1. Introduction

A large body of evidence indicates that higher levels of PA in late life are associated with reduced risks of several chronic diseases and all-cause mortality (Nelson et al., 2007). On the other hand, SED, defined as any waking behavior characterized by an energy expenditure ≤1.5 METs while in a sitting or reclining posture, is increasingly recognized as a life-style factor raising the risk of cardiovascular disease, type 2 diabetes mellitus and mortality, independent of PA levels (Biswas et al., 2015; Chomistek et al., 2013; Koster et al., 2012). Therefore, accurate measurement of the PA and SED levels in community-dwelling older population under free living conditions is needed to improve the understanding of daily PA and SED, and to inform public health strategies to increase PA and reduce SED in older adults.

Traditionally, epidemiological studies rely on subjective measures, such as questionnaires and behavioral records, in the assessment of PA in community-dwelling older people. However, such measures are often reported to either over- or underestimate PA levels due to recall bias, particularly in older adults (Kowalski et al., 2012). Moreover, many of the existing subjective tools fail to measure SED and light-intensity PA adequately (Shephard, 2003), while these two might be major determinants of daily PA level for older adults (Colbert et al., 2014; Meijer et al., 2001).
Alternatively, accelerometers are capable of measuring PA objectively, and thus have been widely accepted as valid measures of PA in a number of populations including older adults (Copeland and Esliger, 2009; Lee and Shiroma, 2014). More recently, a tri-axial accelerometer with its prediction models accounting for the type of activity performed has been shown to yield more accurate estimation of PA intensity (Kumagai et al. 2015; Midorikawa et al., 2007; Ohkawara et al., 2011), which might potentially improve the understanding of daily PA and SED in older adults.

To date, there are only a few large-scale studies that objectively assessed PA and SED using accelerometers in older adults while most of accelerometer-based studies were carried out in the western population (Arnardottir et al., 2013; Davis et al., 2011; Evenson et al., 2012; Hansen et al., 2012; Jefferis et al., 2014; Lohne-Seiler et al., 2014). Little is known regarding accelerometer-derived PA and SED levels in older adults in countries of different cultures and environments, such as Japan. Moreover, although the Japanese society undergoing the world’s fastest aging, Japan has the highest healthy life expectancy at birth (Tamiya et al., 2011). Thus, data from older adults in Japan may provide unique insight into the current levels of PA and SED in older adults. The main aims of this study were therefore to 1) describe levels of PA and SED in Japanese community-dwelling older people, using tri-axial accelerometers, 2) examine the
variation of PA and SED with respect to sex, age, and body mass index (BMI).

2. Method

2-1 Participants

The present study was performed as part of the baseline survey of Sasaguri Genkimon Study (SGS) conducted from May to August 2011. The design of the SGS is described in detail elsewhere (Narazaki et al., 2014; Narazaki et al., 2013). Briefly, it is an ongoing community-based prospective study in the town of Sasaguri, a suburban town on Kyushu Island located in the southwest part of Japan, aiming to explore modifiable lifestyle factors causing older adults to require long-term care. Subjects of the baseline study (SGS-1) were all residents of the town, who were 65 years or older and not certified as individuals requiring long-term care by Japan’s Long-term Care Insurance System (Tsutsui and Muramatsu, 2005) at the end of January 2011 (n=4,979: 15.7% of residents of the town, men: 43.6%). Sixty-six subjects were excluded due to being dead or moving out by the onset of the study. A set of study information sheets and a questionnaire were mailed to all remaining subjects (n = 4,913), and 2,629 individuals, hereafter referred to as the participants of the SGS-1, agreed to take part in SGS-1 by 1) visiting the nearest community center or municipal office of the town, 2)
agreeing to take an individual home-testing session if they were unable to come or not available on the testing day (recruitment rate: 53.5%). All participants of SGS-1 were invited to take part in the study of objectively measured PA during the SGS-1. Of these, we excluded 582 individuals who did not wear the accelerometer, 300 individuals providing less than 4 days of valid accelerometer data, and 8 participants missing BMI data (Figure 1). Given that individuals with long-term care needs were excluded from the SGS during the prescreening process and quality of the accelerometer data depends on participants’ compliance (Wilcox et al., 2002), no additional exclusion criterion was decided to maximize the sample size. Thus, 1,739 participants were included in the present analysis (66.1% of the baseline sample) (Figure 1). All the participants provided written informed consent, and the study was conducted in accordance with the declaration of Helsinki and was approved by the Institutional Review Board of the Institute of Health Science, Kyushu University.
Figure 1. Flow chart of participation

Note: This figure shows the flow of participation in the present study. BMI denoted body mass index.
2-2. Physical activity and sedentary behavior measures

PA was measured by a tri-axial accelerometer (Active style Pro HJA-350IT, Omron Healthcare, Kyoto, Japan). Participants were instructed to wear the accelerometer on either the right or left side of their waist for consecutive 7 days and to remove the accelerometer only before going to bed or water activities. A simple instruction and a log diary were also provided to encourage the compliance to accelerometer protocols.

Technical specification and data acquisition system for the Active style Pro have been previously reported (Ohkawara et al., 2011; Oshima et al., 2010). Briefly, data was collected in 1-minute epochs for the data analysis. An established model, in combination with PA classification algorithm for discrimination between locomotive and non-locomotive activities, was used to estimate the intensity of PA (Ohkawara et al., 2011). METs determined by the Active style Pro have been reported to be closely correlated with METs calculated by the indirect calorimetry, with an average percentage of differences less than 10% (Ohkawara et al., 2011). Accordingly, intensity of PA captured was expressed in METs (Ohkawara et al., 2011). Non-wearing time was defined as at least 60 consecutive minutes of zero counts, with allowance for 2 minutes with counts greater than zero. Data for participants with at least 4 valid wear days (at least 10 hours of wear time per day) were included in the analysis, which is in line with
previous studies to estimate habitual PA in older adults (Arnardottir et al., 2013; Hansen et al., 2012; Lohne-Seiler et al., 2014).

METs-based cut-points were used to define SED, light PA (LPA), and moderate-to-vigorous PA (MVPA) as following: ≤1.5 METs for LPA, 1.6-2.9 METs for LPA, and ≥3 METs for MVPA (Ainsworth et al., 2000; Owen et al., 2010). Number of steps (steps per day) was also calculated using data from the accelerometer. Number of steps and numbers of minutes for the respective activities were summed over valid days, and mean values were then calculated.

2-3. Other measures

Demographic variables including age and sex were provided by the town. Body mass (kg) and height (m) were measured using standard protocols. BMI was calculated as weight mass divided by height squared (kg/m²) and then categorized into two groups: BMI <25 and BMI ≥25. Age was categorized into the following four groups: 65-69, 70-74, 75-79, and 80 years or older.

2-4. Statistical analyses

Descriptive data are presented as mean and SD except where noted. The Mann–Whitney U-test and the chi-square test were conducted to compare age and sex, respectively, between participants of the present study and the rest of the subjects.
including subjects who did not respond to SGS and participants who were excluded from the SGS-1 (n=3,174). The Student’s t-test was used to performed to assess the difference in BMI between the participants of the present study and participants excluded from the SGS-1 (n = 890).

Sex, age, and BMI differences in each of the PA variables were tested by three-way analysis of variance (ANOVA) including all possible interaction terms. Tukey-Kramer post-hoc tests were performed within significant age effects to identify differences across age groups. Because the distributions of time spent in MVPA and number of steps per day were positively skewed, we used a log transformation (log[x]) prior to the analyses. In the descriptive tables and figures, non-transformed data were presented for easy interpretation. A significance level was set at two-sided \( \alpha = 0.05 \). All statistical analyses were conducted using the SAS version 9.3 (SAS Institute Inc., Cary, N.C., USA).

3. Results

The participants of the present study differed from the rest of the subjects in terms of sex (higher percentage of women in the present study, \( p < 0.001 \)), but not in terms of age (\( p = 0.125 \)). Also, BMI was not different between the participants of the present
study and those excluded from the SGS-1 (p = 0.112). The median age (interquartile range or IQR) was 72 (68-79) years and 38.0% of the participants were men. Table 1 presents the characteristics of the present participants and the frequency distribution of the sample by sex, age, and BMI groups.
<table>
<thead>
<tr>
<th></th>
<th>All (n=1739)</th>
<th>Men (n=660)</th>
<th>Women (n=1079)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>72 (68-78)</td>
<td>72 (68-77)</td>
<td>72 (68-78)</td>
</tr>
<tr>
<td><strong>Age groups, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>576 (33.1)</td>
<td>221 (33.5)</td>
<td>355 (32.9)</td>
</tr>
<tr>
<td>70-74</td>
<td>486 (28.0)</td>
<td>192 (29.1)</td>
<td>294 (27.3)</td>
</tr>
<tr>
<td>75-79</td>
<td>371 (21.3)</td>
<td>139 (21.1)</td>
<td>232 (21.5)</td>
</tr>
<tr>
<td>≥80</td>
<td>306 (17.6)</td>
<td>108 (16.4)</td>
<td>198 (18.4)</td>
</tr>
<tr>
<td><strong>BMI, kg/m²</strong></td>
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<tr>
<td><strong>BMI groups, n (%)</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>BMI &lt;25</td>
<td>1308 (75.2)</td>
<td>504 (76.4)</td>
<td>804 (74.5)</td>
</tr>
<tr>
<td>BMI ≥25</td>
<td>431 (24.8)</td>
<td>156 (23.6)</td>
<td>275 (25.5)</td>
</tr>
</tbody>
</table>

*Note:* *Data are represented as median (interquartile range). BMI: body mass index.*
Overall, mean (SD) accelerometer wear time was 13.8 (1.7) hours/day. The average steps/day among participants varied widely (49-20,872 per day). The mean (SD) or median (IQR) of the time spent in SED, LPA and MVPA were 7.5 (2.0) hours, 5.5 (1.6) hours, and 37.8 (19.0-60.7) minutes. Accordingly, the mean (SD) of the proportion of the wear time spent in SED, LPA and MVPA were 54.5% (12.9%), 40.2% (11.1%), and 5.4% (4.0%). Descriptive statistics of the PA by sex, age and BMI groups are presented in Table 2.
Table 2. Tri-axial accelerometer-determined PA and SED by sex, age, and BMI

<table>
<thead>
<tr>
<th></th>
<th>All (n=1739)</th>
<th>Men (n=660)</th>
<th>Women (n=1079)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step (steps/day)</strong>†</td>
<td>4473 (2861-6523)</td>
<td>4615 (2987-6900)</td>
<td>4402 (2797-6356)</td>
<td>0.3529</td>
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<tr>
<td>65-69</td>
<td>5670 (3976-7806)</td>
<td>5767 (4179-8021)</td>
<td>5583 (3815-7527)</td>
<td>&lt;.0001^</td>
</tr>
<tr>
<td>70-74</td>
<td>4795 (3301-6600)</td>
<td>4550 (3229-6538)</td>
<td>4925 (3374-6713)</td>
<td></td>
</tr>
<tr>
<td>75-79</td>
<td>3986 (2468-5609)</td>
<td>4174 (2655-6101)</td>
<td>3778 (2407-5565)</td>
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<td>≥80</td>
<td>2561 (1396-4089)</td>
<td>2986 (1694-4716)</td>
<td>2436 (1351-3729)</td>
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<tr>
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<td>4542 (2922-6672)</td>
<td>4757 (3014-7084)</td>
<td>4409 (2818-6426)</td>
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<tr>
<td>BMI ≥25</td>
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<td>4229 (2779-6191)</td>
<td>4295 (2720-6042)</td>
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<tr>
<td><strong>SED (minutes/day)</strong></td>
<td>451.6 (122.4)</td>
<td>485.4 (129.6)</td>
<td>431.0 (113.0)</td>
<td>&lt;.0001^</td>
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<tr>
<td>65-69</td>
<td>430.8 (122.0)</td>
<td>458.5 (132.6)</td>
<td>413.6 (111.6)</td>
<td>&lt;.0001^</td>
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<td>492.6 (137.0)</td>
<td>424.8 (106.9)</td>
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<td>433.5 (110.4)</td>
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<td>≥80</td>
<td>485.3 (122.4)</td>
<td>516.7 (122.4)</td>
<td>468.2 (119.2)</td>
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</tr>
<tr>
<td>BMI &lt;25</td>
<td>446.6 (122.5)</td>
<td>482.2 (128.9)</td>
<td>424.3 (112.8)</td>
<td>&lt;.0001^</td>
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<td>BMI ≥25</td>
<td>466.8 (120.9)</td>
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<td>450.4 (111.5)</td>
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<tr>
<td><strong>LPA (minutes/day)</strong></td>
<td>332.5 (98.1)</td>
<td>278.8 (89.3)</td>
<td>365.3 (88.3)</td>
<td>&lt;.0001^</td>
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<td><strong>Age groups</strong></td>
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<td>65-69</td>
<td>350.8 (96.3)</td>
<td>297.2 (88.9)</td>
<td>384.2 (85.1)</td>
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<td>70-74</td>
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<td>BMI &lt;25</td>
<td>338.2 (98.0)</td>
<td>284.0 (87.9)</td>
<td>372.1 (88.3)</td>
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<td>BMI ≥25</td>
<td>315.1 (96.5)</td>
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<td>345.3 (85.5)</td>
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<tr>
<td><strong>MVPA (minutes/day)</strong></td>
<td>37.8 (19.0-60.7)</td>
<td>33.7 (16.8-57.9)</td>
<td>40.0 (20.2-63.3)</td>
<td>&lt;.0001^</td>
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<td><strong>Age groups</strong></td>
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<td>65-69</td>
<td>54.2 (33.6-78.1)</td>
<td>53.3 (31.0-69.8)</td>
<td>54.9 (35.6-83.8)</td>
<td>&lt;.0001^</td>
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<td>39.7 (23.3-58.8)</td>
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<td>40.8 (26.8-66.0)</td>
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<td>31.0 (14.6-50.6)</td>
<td>25.9 (13.0-44.0)</td>
<td>33.3 (15.9-55.1)</td>
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<tr>
<td>≥80</td>
<td>16.8 (7.6-34.5)</td>
<td>14.2 (7.1-32.1)</td>
<td>18.5 (7.7-34.8)</td>
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<td><strong>BMI groups</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>BMI &lt;25</td>
<td>38.9 (19.4-62.8)</td>
<td>34.6 (17.1-59.3)</td>
<td>41.3 (20.5-66.1)</td>
<td>0.0408^</td>
</tr>
<tr>
<td>BMI ≥25</td>
<td>35.8 (17.5-56.4)</td>
<td>32.1 (15.7-49.9)</td>
<td>37.1 (19.4-59.3)</td>
<td></td>
</tr>
</tbody>
</table>

Note: Data are represented as median (interquartile range) or Mean (SD). ^ Significant difference among age groups.  b Significant difference between BMI groups.  c Significant difference between sexes.  † Significant age×BMI interaction effect. PA, physical activity; SED, sedentary behavior; BMI, body mass index; LPA, light physical activity; MVPA, moderate-to-vigorous physical activity.
Results of ANOVA indicated significant age and BMI effects in steps/day, while there was no main effect for sex (p = 0.3529) (Table 2). Only one significant interactive effect was observed in steps/day: age × BMI (F=3.18, p<0.05) (Table 2). Post hoc comparisons showed significant difference between all age groups except between 70-74-yr and 75-79-yr age groups in higher BMI group. Within age groups, lower BMI group accumulated more steps/day than higher BMI group only in the oldest age groups (Figure 2).
Figure 2. Mean steps/day by age and BMI groups

Note: Columns are means and standard deviation. BMI denoted body mass index.
There were significant gender, age, and BMI effects in SED and PA of different intensities (LPA and MVPA), and no significant interactive effects were observed (Table 2). Men had longer SED (F=91.10, p<0.0001), and accumulated fewer minutes of LPA and MVPA (F=422.97, p<0.0001, and F=18.09, p<0.0001, respectively) than women. There was significantly shorter SED in lower BMI group compared with higher BMI group (F=11.12, p<0.001). In contrast, time spent in LPA and MVPA were higher in lower BMI group compared with the higher BMI group (F=28.28, p<0.0001, and F=4.19, p<0.05, respectively). Post hoc comparisons showed that the oldest age group spent significantly longer time in sedentary time and shorter time in LPA than other 3 age groups (Figure 3A and B, respectively). There was a marked decline in time spent in MVPA across the age groups, with significant differences between all age groups (Figure 3C).
Figure 3. Mean minutes spent in SED, LPA, and MVPA by age groups

Note: Columns are means and standard deviation.* Significantly (p <0.05) different from the 65-69-yr age group. † Significantly (p <0.05) different from the 70-74-yr age group. ‡ Significantly (p <0.05) different from the 75-79-yr age group. §Significantly (p <0.05) different from the ≥80-yr age group. SED: sedentary behavior, LPA: light physical activity, MVPA: moderate-to-vigorous physical activity.
4. Discussion

The present study included a larger sample than previous Japanese older adults based studies of objectively measured PA (Osuka et al., 2014; Yasunaga et al., 2008), and to our knowledge, is the first one to objectively measure SED using tri-axial accelerometer in community-dwelling older adults in Japan. The present study shows that the older adults spent 54.5% of their waking time being sedentary and 40.2% as LPA, while only a small proportion of the active time was spent in MVPA. Overall, median MVPA (IQR) was 33.7 (16.8-57.9) and 40.0 (20.2-63.3) minutes per day in men and women, respectively. The PA levels were lower and SED was longer with age. Furthermore, participants with higher BMI had lower PA levels, and longer SED than participants with lower BMI. In contrast with previous observations in western populations (Arnardottir et al., 2013; Davis et al., 2011; Evenson et al., 2012; Jefferis et al., 2014), women spent less time in SED and more time in LPA and MVPA than men in the present study. In light of this, the commonly accepted assumption that men are more active than women might be not the case in Japanese older population.

On average, men took 5,201 steps/day and women took 4,771 steps/day in the present study which were slightly higher than accelerometer-determined data observed in UK (Davis et al. 2011) and U.S. older adults (Tudor-Locke et al., 2013). In the Nakanojo
Study, among 95 Japanese older adults, both men and women took much higher yearlong-averaged steps/day than data reported in the present study, which may explained by their convenience sampling method (Yasunaga et al., 2008). With respect to intensity distribution, the participants in the present study spent 7.5 hours (54.5%) in SED, 5.5 hours (40.2%) in LPA, and 44.6 minutes (5.4%) in MVPA. Based on the observed results, participants in the present study appeared to be somewhat more active than that have been reported in Iceland (Arnardottir et al., 2013) and Norway (Lohne-Seiler et al., 2014), in terms of smaller proportion of SED and greater proportion of LPA and MVPA. However, direct comparison between the present study and previous studies is somewhat problematic, because of existence of regional difference, the use of different methods, and more specifically different accelerometers and differences in data processing procedures. To date, most accelerometers in previous studies recorded acceleration data only from the vertical axis. A cut-point approach, which is developed from a single calibration equation, has been extensively used to distinguish intensity categories (e.g., LPA and MVPA) (Freedson et al., 1998; Hendelman et al., 2000). Unfortunately, much of the equation has derived only from locomotive activities, which was found to significantly underestimate the intensity of most lifestyle activities (e.g., laundry, cooking, vacuuming) (Bassett et al., 2000;
Hendelman et al., 2000). On the other hand, the equations developed on moderate-intensity lifestyle activities tended to overestimate sedentary and light activities (Crouter et al., 2006). In contrast, the Active style Pro has been used in combination with its PA classification model developed from the synthetic acceleration of all three axes (anterior-posterior, mediolateral, and vertical direction), and thus provided a substantial improvement compared to non-classification model for estimating the intensity of various PA, accuracy improvements occurred for household activities in particular (Ohkawara et al., 2011). Given that the majority of activities in older adults is LPA and comes from daily life, the tri-axial accelerometer used in the present study would allow for more accurate estimation of daily activities in older adults.

Based on studies conducted in western populations (Arnardottir et al., 2013; Davis et al., 2011; Evenson et al., 2012; Jefferis et al., 2014), the bulk of the literature supports a higher level of PA among men. In contrast with previous observations, the present study showed that women were more active than men, in terms of time spent in MVPA. As indicated above, one explanation for the discrepancy in sex differences is the different methodologies used to quantify PA. In consideration of traditional gender roles, women are more involved in household activities, intensity of which would have formerly been...
underestimated (Bassett et al., 2000; Hendelman et al., 2000). Indeed, some of the household activities are applicable to activities above 3 METs, such as vacuuming, sweeping and mopping (Bassett et al., 2000). Thus, it is conceivable that the underestimated intensities of household activities might lead to underestimating MVPA in women in previous studies. Furthermore, Japanese older women may spend more time in household activities than western older women. According to the NHK (Nippon Hoso Kyokai, a Japan's national public broadcasting organization) National Time Use survey, over 88% of Japanese older women carried out housework on every day of the week, while that for older men were far lower than women, which were less than 59% on weekdays, less than 62% on Saturdays, and less than 58% on Sundays (Kobayashi et al., 2011). Accordingly, women spend substantially more time in housework than men, which may be a possible explanation for the observation in the present study that women spent more time in MVPA compared with men. Therefore, difference of lifestyle of older women between Japan and western population may also partly explain the discrepancy in sex differences in PA levels. The substantially higher LPA and lower SED in women than men observed in the present study, which are consistent with previous studies (Arnardottir et al., 2013; Davis et al., 2011; Hansen et al., 2012; Jefferis et al., 2014; Lohne-Seiler et al., 2014). Moreover, the non-significant difference
in daily steps between the sexes observed in the present study suggests that, in addition to locomotive activities (e.g., walking, jogging), lifestyle activities may play a significant role to overall PA levels in women.

Consistent with previous studies (Arnardottir et al., 2013; Davis et al., 2011; Hansen et al., 2012; Lohne-Seiler et al., 2014), higher age is related to lower levels of PA and longer SED. A sharp decline in MVPA was observed across the age groups, which is not surprising, as the aging process along with functional limitations and health conditions may limit the ability to engage in or maintain MVPA (Brawley et al., 2003). In contrast, LPA remained relatively stable until age 80-yr, which seems to correspond with the observed age-related increase in SED. We could speculate that those spent less time in LPA may, therefore, spend more time in SED. Given recent findings by Buman et al. (2010) showing significant associations of objectively measured LPA with both physical and psychosocial well-being in older adults, replacing SED by LPA may be a practical and meaningful intervention strategy designed to increase PA levels for older adults.

In regard to BMI and PA, participants with higher BMI had fewer LPA and MVPA, and longer SED compared with those with lower BMI. These findings are consistent with existing cross-sectional data that showed lower PA levels and longer SED with
increasing BMI (Arnardottir et al., 2013; Davis et al., 2011). In the present study, the difference in daily steps between BMI categories was observed only in the oldest age group. Given the different levels of PA and SED between BMI categories in the present study, BMI should be taken into account in the future PA interventions study in the Japanese old adults, especially for the oldest older group.

The major strength of the present study is the use of tri-axial accelerometer to assess PA and SED, which allowed for a more accurate estimate of PA intensity compared with a conventional uni-axial accelerometer (Midorikawa et al. 2007; Ohkawara et al., 2011). An additional strength is that the present report is based on a relatively large population-based cohort of older Japanese adults, which is a population of particular public health interest given the Japanese society undergoing the world’s fastest aging with the highest health life expectancy (Tamiya et al., 2011). Limitations of the present study should also be considered in the interpretation of our findings. First, the sample of the present study was affected to some extent by the nonresponse, withdrawal and exclusion of originally designated subjects, which may reduce the potential for generalization. However, there was no age or BMI bias. Moreover, men included in the present study had better physical and cognitive function than those excluded from SGS-1 (data not shown). PA levels might be somewhat overestimated in men, thus it is
reasonable to assume that higher response rate in women would not affect the sex-differences in PA levels. Second, it is known that limitations of accelerometers include their inability to detect some type of PA, such as water activities and cycling, thus these activities are likely to be missed or underestimated. However, such kinds of activities were not common according to the self-reported questionnaires in the present cohort (data not shown), which may diminishes the possibility that PA level was underestimated.

5. Conclusion

In summary, the present study first demonstrated PA levels and SED differed by sex, age, and BMI in Japanese community-dwelling older adults. The results also showed a high level of SED and low level of PA in the Japanese older population. Further research including a wider range of socio-demographic, psychological and environmental factors is recommended to provide a more comprehensive understanding of the determines of PA and SED in older adults, which will benefit the development of effective population-based intervention strategies to increase PA and reduce prolonged SED in the Japanese population and possibly other rapidly aging societies.
Chapter 3. Associations of tri-axial accelerometer-determined sedentary time and breaks in sedentary time with disability in instrumental activities of daily living in community-dwelling older adults (Study 2)
1. Introduction

Functional disability in older adults is an important risk factor for institutionalization (Luppa et al., 2010) and mortality (Millán-Calenti et al., 2010), and places a large burden on the public health and social services (Fried et al., 2001). Functional disability is commonly assessed by the BADL (including basic self-care function, such as eating and dressing) and/or IADL (including more-complex tasks, such as household chores and shopping). IADL, which includes the most relevant capacities for living independently in a community, its impairment has been reported to predict future onset of BADL disability (Reynolds et al., 2003). Furthermore, given the hierarchical relationship between BADL and IADL disability, IADL disability usually precedes BADL disability (Nourhashe´mi et al., 2001). In other words, people disabled in BADL also would be already disabled in IADL, but not vice versa. Therefore, identifying modifiable risk factors for IADL disability in relatively functional older adults is a critical step in the primary prevention of subsequent BADL disability and other adverse outcomes.

Substantial evidence has shown that MVPA has a beneficial effect on maintaining functional capacity and reduces the risk of disability in older adults (Paterson et al., 2010; Dunlop et al., 2014). In contrast, emerging evidence suggests that, in addition to
MVPA, SED, defined as activities such as sitting and lying down that do not increase energy expenditure substantially above the resting level (≤1.5 METs) (Pate et al., 2008), is associated with reduced muscle mass (Gianoudis et al., 2015), lower physical function (Davis et al., 2014; Santos et al., 2012; Sardinha et al., 2015), and higher risk of BADL and IADL disability (Cawthon et al., 2013). Importantly, the association between objectively measured sedentary time (ST) and lower physical function is independent of MVPA (Davis et al., 2014; Santos et al., 2012; Sardinha et al., 2015), which is consistent with the novel idea that sedentary behavior is a distinct concept from insufficient MVPA and has independent effects on health outcomes (Tremblay et al., 2010). However, whether ST is independently associated with IADL disability remains uncertain.

More recently, there is some evidence that greater number of breaks in sedentary time (BST: defined as at least 1 minute where the intensity of activity rose up to or above 1.5 METs following a sedentary bout) are beneficially associated with lower extremity function and overall physical function in older adults, independent of total ST and MVPA (Davis et al., 2014; Sardinha et al., 2015). Given that lower extremity function and overall physical function are important to maintain functional capacity of older adults, and useful predictors of disability in older adults (Guralnik et al., 1995; Idland et
These findings highlight that not only total ST, but also the BST may be one of the critical factors determining late-life functional capacity.

To our knowledge, no studies have investigated if ST and BST would be associated with IADL disability independent of MVPA, and whether the association for ST was independent of BST, and vice versa. These questions are important from public health perspective because current physical activity (PA) guidelines for maintaining functional capacity and preventing disability in older adults focus exclusively on MVPA but appear to ignore the potential adverse effects of sedentary behavior, while older adults are the most sedentary compared with younger age group. The aim of the present study was therefore to investigate the associations of objectively measured ST and BST with IADL disability in community-dwelling older adults. We hypothesized that shorter ST and greater number of BST would be related to lower risk of IADL disability after controlling for MVPA, and that the association for ST was independent of BST, and vice versa.

2. Method

2-1. Participants

The present study was performed as part of SGS-1 conducted from May to August
2011. The design of the SGS is described in detail elsewhere (Narazaki et al., 2013). Briefly, it is an ongoing community-based prospective study in Sasaguri town, a suburban town located in the southwest part of Japan, aiming to explore modifiable lifestyle factors causing older adults to require long-term care. Subjects of the baseline study were 2,629 residents of the town, who were 65 years or older and not certified as individuals requiring long-term care by Japan’s Long-term Care Insurance System at the end of January 2011. Of these, we excluded 17 individuals with medical history of dementia or Parkinson’s disease and 74 individuals with mobility limitation (inability to walk 45 meter) or severely limited BADL (≤60 on the Barthel Index) (Arai et al., 2000); also excluded 817 individuals who did not have valid accelerometer data, 2 participants without complete data on IADL, and 85 individuals with missing data on the covariates (Figure 4). Thus, 1,634 participants were included in the present analysis (62.2% of the baseline sample). Compared with the subjects excluded from the baseline sample (n=995), participants in the present study had a lower proportion of men, were younger, and had higher BMI, higher rate of living alone, lower rate of having stair climbing difficulty and distress, better self-rated health, better cognitive function, lower rate of current smoker, higher IADL score and a lower rate of IADL disability, but otherwise was similar in years of education and rate of multimorbidity (Supplementary Table 1).
All the participants provided written informed consent, and the study was conducted in accordance with the declaration of Helsinki and was approved by the Institutional Review Board of the Institute of Health Science, Kyushu University.
Figure 4. Flow chart of participation

Note: This figure shows the flow of participation in the present study. ADL, activities of daily living; IADL, instrumental activities of daily living; BMI, body mass index.
2-2. Sedentary behavior and physical activity measures

Participants were instructed to wear a tri-axial accelerometer (Active style Pro HJA-350IT, Omron Healthcare, Kyoto, Japan) on either side of their waist for consecutive 7 days and to remove the accelerometer only before going to bed or water activities. A simple instruction and a log diary were also provided to encourage the compliance to accelerometer protocols. Data was collected in 1-minute epochs for the analysis. Intensity of minute-by-minute activity was estimated by built-in algorithms containing a specific equation for sedentary activities (Ohkawara et al., 2011). METs determined by the Active style Pro have been validated with the Douglas bag method (Ohkawara et al., 2011). The SAS macro program provided by the National Institute of Cancer was used to compute non-wear time, with modifications based on our accelerometer (National Cancer Institute, 2007). Non-wear time was defined as at least 60 consecutive minutes of no activity (i.e., estimated activity intensity <1.0 METs), with allowance for 2 minutes of activities with intensity rose up to 1.0 METs (Honda et al., 2014). Data for participants with at least 4 valid wear days (at least 10 hours of wear time per day) were included in the analysis (Arnardottir et al., 2013).

The cutoff values used to define time spent in ST and MVPA were as the following: ≤1.5 METs for ST (Pate et al., 2008) and ≥3 METs for MVPA. BST was defined as at
least 1 minute where the intensity of activity rose up to or above 1.5 METs following a sedentary bout (Davis et al., 2014; Sardinha et al., 2015). ST, MVPA and number of BST were averaged across valid days to obtain daily mean values. ST and number of BST were adjusted for wear time by regressing these variables on wear time and residuals from the models represented adjusted variables to account for variability in daily monitoring time (Sardinha et al., 2015; Willett et al., 1997).

2-3. Disability in instrumental activities of daily living measures

IADL was measured using a five-item subscale of Instrumental Self-Maintenance of the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC) (Koyano et al., 1991). The Index itself consists of total 13 items and allots five items to IADL measures including using public transportation, shopping for daily necessities, preparing meals, paying bills and handling a bank account. Responses to each item were scored either 1 point (able to do) or 0 point (unable to do). The IADL score ranged from 0 to 5 points, with a lower score indicating greater number of IADL disability. Subjects with a total score <5 were defined as having IADL disability (Ishizaki et al., 2002).

2-4. Covariates measurements

Demographic variables including age and sex were provided by the town. Years of formal education, living alone (yes or no), and current smoking (yes or no) were
obtained from a questionnaire. Body mass (kg) and height (m) were measured using conventional scales, and BMI was calculated by dividing the body mass by height squared (kg/m^2). Multimorbidity was defined as the presence of ≥2 chronic diseases out of 13 chronic diseases: hypertension, stroke, heart disease, diabetes mellitus, lipid abnormality, respiratory disease, digestive disease, kidney disease, osteoarthritis or rheumatism, trauma fracture, cancer, ear disease, and eye disease. The presence of chronic diseases was self-reported in the questionnaire. Self-rated health was assessed by the question “How would you rate your current overall health?” with responses of “very good”, “good”, “fair”, and “poor”. Responses were dichotomized as very good/good and fair/poor. Psychological distress was measured by the Japanese version of the Kessler 6 psychological distress scale (K6) in the questionnaire (Sakurai et al., 2011). Participants who scored 5 points or more on the scale were classified as having psychological distress. In the present study, the K6 scores were used in logistic analyses while the psychological distress status was reported in demographic description. Cognitive function was measured with the Japanese version of the Montreal Cognitive Assessment (MoCA-J) (Fujiwara et al., 2010). MoCA-J scores range from 0-30 with higher scores indicating better cognitive function. Although we have excluded participants who have mobility limitation and severely limited BADL, stair climbing
difficulty, which is one of the items in Barthel Index of BADL (Shah et al., 1989), was used to rule out the confounding effect of unmeasured lower extremity limitation. For the present study, responses to stair climbing were dichotomized as “unable to do at all/need some help” and “without help”, where the former answer referred to “stair climbing difficulty”.

2-5 Statistical analyses

All statistical analyses were conducted using the SAS version 9.3 (SAS Institute Inc., Cary, N.C., USA). A significance level was set at two-sided $\alpha = 0.05$. Mean (SD) was calculated for continuous variables, and frequency (%) for categorical variables. Characteristics of participants were compared between groups according to IADL disability status, using chi-square test and Student’s t-test as appropriate.

Multiple logistic regression models were used to examine the associations of ST and BST with IADL disability. ST and BST were used as continuous standardized z-scores (mean=0, SD=1) in the models, with OR expressed per 1-SD increment in the sedentary variables. The first model was adjusted for sex and age. In the second model, we additionally adjusted for years of formal education, BMI, living status, multimorbidity, stair climbing difficulty, self-rated health, MoCA-J, K6, and smoking status as covariates. The third model was further adjusted for MVPA to examine whether the
associations were independent of MVPA. Furthermore, we examined the independent association of ST and BST with IADL disability by mutually adjusting models for both factors. Bivariate correlations between MVPA, ST and BST were relatively low (MVPA vs. ST, Spearman’s $\rho = -0.42$; MVPA vs. BST, Spearman’s $\rho = 0.01$; ST vs. BST, Spearman’s $\rho = 0.07$) and the variance inflation factors were <2 in each model indicating that there was no evidence of multicollinearity. Additionally, we tested the interactions between sex, age, and MVPA (<30 or $\geq$30 minutes/day) with each of ST and BST in each model, to examine potential effect moderation by sex, age and MVPA.

Sensitivity analyses were conducted to investigate whether results were affected by 90-minute non-wear criterion with allowance for 2 minutes for interruptions, which have been recommended to improve the accuracy of wear time and ST estimates for tri-axial accelerometer in free-living older adults (Choi et al., 2012). As sensitivity analyses, the logistic regression models were repeated using sedentary variables estimated by the 90-minute non-wear criterion.

3. Results

Descriptive characteristics of the 1,634 participants are presented in Table 3. The mean age (SD) of the sample was 73.3 (6.0) years and 38.4% were men. Participants
wore the accelerometer for a mean (SD) of 14.0 (1.8) hours per day over a mean (SD) of 7.1 (1.3) days. The mean (SD) of the time spent in sedentary behavior and MVPA were 463.0 (125.4) minutes per day and 45.0 (34.5) minutes per day, respectively. The mean (SD) number of BST was 59.0 (13.2) times per day.
### Table 3. Characteristics of subjects by IADL disability

<table>
<thead>
<tr>
<th></th>
<th>Total (n=1,634)</th>
<th>Disability in IADL</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=137)</td>
<td>No (n=1,497)</td>
<td></td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>627 (38.4)</td>
<td>523 (34.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age, years</td>
<td>73.3 (6.0)</td>
<td>73.1 (5.8)</td>
<td>0.002</td>
</tr>
<tr>
<td>Education, years</td>
<td>11.1 (2.4)</td>
<td>11.2 (2.4)</td>
<td>0.010</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.2 (3.1)</td>
<td>23.2 (3.1)</td>
<td>0.510</td>
</tr>
<tr>
<td>Living alone, n (%)</td>
<td>217 (13.3)</td>
<td>211 (14.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Multimorbidity, n (%)</td>
<td>747 (45.7)</td>
<td>671 (44.8)</td>
<td>0.017</td>
</tr>
<tr>
<td>Stair climbing difficulty, n (%)</td>
<td>35 (2.1)</td>
<td>23 (1.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Psychological distress (K6 ≥5), n (%)</td>
<td>465 (28.5)</td>
<td>411 (27.5)</td>
<td>0.003</td>
</tr>
<tr>
<td>Self-rated health (fair/poor), n (%)</td>
<td>317 (19.4)</td>
<td>280 (18.7)</td>
<td>0.019</td>
</tr>
<tr>
<td>MoCA-J, points</td>
<td>22.2 (3.8)</td>
<td>22.3 (3.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>120 (7.3)</td>
<td>101 (6.8)</td>
<td>0.002</td>
</tr>
<tr>
<td>Accelerometer wear time, hours/day</td>
<td>14.0 (1.8)</td>
<td>14.0 (1.8)</td>
<td>0.274</td>
</tr>
<tr>
<td>MVPA, minutes/day</td>
<td>45.0 (34.5)</td>
<td>46.1 (34.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ST, minutes/day</td>
<td>463.0 (125.4)</td>
<td>457.5 (122.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BST, times/day</td>
<td>59.0 (13.2)</td>
<td>59.4 (13.1)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Note: Data are represented as mean (SD) or n (%). * Statistical significance based on chi-square tests or t-tests, as appropriate. IADL, instrumental activities of daily living; BMI, body mass index; K6, Japanese version of the Kessler 6 psychological distress scale; MoCA-J, Japanese version of the Montreal Cognitive Assessment; MVPA, moderate-vigorous physical activity; ST, sedentary time; BST, breaks in sedentary time.
Of the total sample, 137 (8.4%) reported IADL disability. Compared with participants independent in IADL, those with IADL disability were more likely to be older, men, less educated, less likely to live alone, having multimorbidity, stair climbing difficulty, distress, poor self-rated health and cognitive function, and more like to be current smoker, having less MVPA, longer ST and fewer number of BST per day (Table 3).

The OR and its 95% CI for IADL disability per 1-SD difference in ST and BST were presented in Table 4. Model 1, adjusted for age and sex, showed the higher likelihood of IADL disability for 1-SD increment in ST, whereas 1-SD increment in BST was associated with lower likelihood of IADL disability. ST and BST remained significantly associated with IADL disability after additional adjustment for other confounding factors in model 2 and MVPA in model 3. In model 3, 1-SD increment in ST per day significantly increased the odds of IADL disability (OR: 1.49, 95% CI: 1.16-1.89). In contrast, the OR of IADL disability per 1-SD increase in BST was 0.73 (95% CI: 0.61-0.88). In model 4, ST and BST remained statistically significant after mutual adjustment with OR of 1.30 (95% CI, 1.00-1.70) and 0.80 (95% CI, 0.65-0.99), respectively. In addition, no significant interactions between sex, age, and MVPA and each of ST and BST were found, suggesting that these factors did not moderate the associations of sedentary behavior and IADL disability.
Table 4. Associations between ST and BST with IADL disability

<table>
<thead>
<tr>
<th></th>
<th>ST per 1-SD increment</th>
<th>BST per 1-SD increment</th>
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<tbody>
<tr>
<td></td>
<td>Odds ratio (95% confidence interval)</td>
<td>Odds ratio (95% confidence interval)</td>
</tr>
<tr>
<td></td>
<td>Model 1(^a)</td>
<td>Model 2(^b)</td>
</tr>
<tr>
<td>ST per 1-SD increment</td>
<td>1.49(^*) (1.22-1.83)</td>
<td>1.50(^*) (1.21-1.87)</td>
</tr>
<tr>
<td>BST per 1-SD increment</td>
<td>0.75(^*) (0.63-0.90)</td>
<td>0.76(^*) (0.63-0.91)</td>
</tr>
</tbody>
</table>

Note: 1-SD for ST and BST are 106.7 minutes/day and 11.7 times/day. ST and BST were adjusted for wear time using the residual method prior to standardization. * Significant at p <0.05. \(^a\) Model 1 adjusted for sex and age. \(^b\) Model 2 adjusted for other confounding factors (years of education, body mass index, living status, multimorbidity, stair climbing difficulty, score of Japanese version of the Kessler 6 psychological distress scale, self-rated health, score of Japanese version of the Montreal Cognitive Assessment, and smoking habit) plus factors in Model 1 as covariates. \(^c\) Model 3 adjusted for moderate-to-vigorous physical activity plus factors in Model 2 as a covariate. \(^d\) Model4 adjusted for factors in Model 3 plus BST or ST, appropriately. ST, sedentary time (adjusted for wear time); BST, breaks in sedentary time (adjusted for wear time); IADL, instrumental activities of daily living; SD, standard deviation.
The number of participants meeting the wear time requirement and other inclusion criteria increased from 1,634 with the 60-minute non-wear criterion to 1,659 (142 participants with IADL disability) with the 90-minute non-wear criterion. The pattern of results and significance levels were comparable with the original associations shown in Table 4 (OR for ST: 1.31, 95% CI: 1.01-1.70; OR for BST: 0.79, 95% CI: 0.64-0.97 in model 4) (Supplementary Table 2).

4. Discussion

The present study examined the associations of objectively measured ST and BST with IADL disability in Japanese community-dwelling older adults. The main findings of the present study are that shorter ST and greater number of BST were related to lower risk of IADL disability after controlling for MVPA, and that the association for ST was independent of BST, and vice versa. These findings suggest not only total ST but also the manner in which it is accumulated may contribute the maintenance of functional capacity in older adults.

Sedentary behavior, such as sitting, is increasingly recognized as a life-style factor raising the risk of cardiovascular disease, type 2 diabetes and mortality, independent of PA levels (Biswas et al., 2015; Chomistek et al., 2013; Koster et al., 2012). With regard
to functional disability, only two recent studies have identified the association between sedentary behavior and disability in older adults (Cawthon et al., 2013; Dunlop et al., 2015). A cross-sectional study using data from the 2003-2005 U.S. National Health and Examination Surveys examined the association between ST and the BADL disability in 2,286 adults aged 60 years and older (Dunlop et al., 2015). They found a strong relationship between greater time spent in sedentary behavior and the presence of BADL disability, independent of time spent in MVPA. Cawthon et al. (2013) used a longitudinal design with 1,983 older men, found that those with greater ST at baseline were more likely to develop a disability in BADL or IADL over a 2-year follow-up. However, it is important to notice that Cawthon et al. (2013) have not controlled for MVPA when investigating the associations, and neither study included BST in their analyses. Our present findings confirm and extend previous findings that ST was associated with IADL disability, independent of BST and MVPA.

To our knowledge, the present study is the first one to demonstrate that objectively measured BST is associated to the IADL disability. Importantly, these associations persisted after controlling for total ST and MVPA, suggesting that frequent BST may impart unique benefit to maintaining functional capacity in older adults. Indeed, two recent cross-sectional studies have shown the beneficial associations between BST and
physical function in older adults (Davis et al., 2014; Sardinha et al., 2015), which may partly explain the independent association between BST and IADL disability. In one study from the Project Older people and Active living, Davis et al. (2014) showed that BST were strongly associated with the lower extremity function assessed by the Short Physical Performance Battery in a diverse sample aged ≥70, independent of total ST and MVPA. In addition, Sardinha et al. (2015) also showed BST predicted overall physical function measured by the Senior Fitness Test and were associated with higher scores in specific fitness parameters like upper and lower body strength, independent of total ST and MVPA. Davis et al. (2014) suggested that even brief BST might be sufficient to trigger certain biomechanical, physiological and neurological response, which may favorably influence functional capacity, but further studies are need to test this hypothesis. Nevertheless, the present findings, coupled with recent findings, further suggest that BST, in addition to total ST, may be also an important factor for maintaining functional capacity in older adults, independent of MVPA.

From a public health viewpoint, findings from the present study have several important implications because current PA guidelines for maintaining functional capacity and preventing disability in older adults recommend MVPA but there are no guidelines targeting sedentary behavior. First, the independent association of ST with
IADL disability found in the present study supports recent findings that sedentary behavior is a distinct health risk factor from the absence of MVPA in older adults and highlights the need of promotion of reduction of ST to avoid too much sitting even in those who have met the PA guideline of 30 minutes MVPA per day. Next, the present study also provides novel evidence that BST, in addition to total ST, may be also an important factor in the prevention of IADL disability. It is worthy to note that a sedentary break could be as short as 1 minute, suggesting that regular breaks from ST probably be a promising intervention strategy for reducing IADL disability in real-life setting in older adults, particularly in physically inactive individuals. Taking together, in the absence of randomized clinical trials, findings in the present study provide preliminary evidence that may inform the development of guidelines and lifestyle strategies related sedentary behavior to maintain functional capacity and prevent disability in older adults.

The strengths of the present study are relatively large population-based sample, the use of a tri-axial accelerometer to objectively assess PA and sedentary behavior, and the adjustment of variety of confounding factors such as cognitive function, psychological distress, self-rated health, multimorbidity and lower extremity limitation. There is no gold-standard criterion to define non-wear time, however, the most commonly used
60-minute non-wear criterion and a longer time widow (90-minute) yielded similar results, suggesting although the criterion used in the present study may be not ideal, it was unlikely to influence the association with IADL disability. Limitations of the present study should also be considered in the interpretation of our findings. First, the cross-sectional design of the present study does not allow conclusions on the direction of causality of these associations. Second, there may have been some selection bias as a large proportion of participants were excluded, mainly because of lacking valid accelerometer data. However, since the excluded subjects presumably spent more ST than the present participants besides the lower functional capacity (Supplementary Table 1), these results may not overestimate the magnitude of the associations of ST and BST with IADL disability. Third, although a variety of confounders were considered, we cannot rule out the possible residual confounding from potentially important unmeasured covariates like pain complaint. Finally, it is known that limitations of accelerometers include their inability to detect some types of PA (e.g., water activities and cycling) and distinguish between postures (e.g., sitting or standing).

5. Conclusion

In conclusion, the present study first demonstrated the independent associations of ST
and BST with IADL disability in Japanese community-dwelling older adults, independent of MVPA and other covariates. These findings support a public health focus on reducing prolonged periods of ST and increasing frequencies of BST alongside promotion PA in older adults. Additional randomized controlled trials are needed to confirm the associations found in the present study.
Supplementary Table 1. Comparisons between the analytic and excluded sample in present study

<table>
<thead>
<tr>
<th></th>
<th>No. of missing</th>
<th>Analytic sample</th>
<th>Excluded sample</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>-</td>
<td>1,634</td>
<td>995</td>
<td>-</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>0</td>
<td>627 (38.4)</td>
<td>520 (52.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age, years</td>
<td>0</td>
<td>73.3 (6.0)</td>
<td>73.9 (6.6)</td>
<td>0.010</td>
</tr>
<tr>
<td>Education, years</td>
<td>44</td>
<td>11.1 (2.4)</td>
<td>11.0 (2.7)</td>
<td>0.172</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>67</td>
<td>23.2 (3.1)</td>
<td>22.9 (3.3)</td>
<td>0.046</td>
</tr>
<tr>
<td>Living alone, n (%)</td>
<td>25</td>
<td>217 (13.3)</td>
<td>101 (10.4)</td>
<td>0.031</td>
</tr>
<tr>
<td>Multimorbidity, n (%)</td>
<td>0</td>
<td>747 (45.7)</td>
<td>417 (41.9)</td>
<td>0.057</td>
</tr>
<tr>
<td>Stair climbing difficulty, n (%)</td>
<td>26</td>
<td>35 (2.1)</td>
<td>64 (6.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Psychological distress (K6 ≥5), n (%)</td>
<td>511</td>
<td>465 (28.5)</td>
<td>167 (34.5)</td>
<td>0.011</td>
</tr>
<tr>
<td>Self-rated health (fair/poor), n (%)</td>
<td>46</td>
<td>317 (19.4)</td>
<td>245 (25.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MoCA-J, points</td>
<td>532</td>
<td>22.2 (3.8)</td>
<td>20.1 (4.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>42</td>
<td>120 (7.3)</td>
<td>133 (14.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IADL score, points</td>
<td>43</td>
<td>4.9 (0.4)</td>
<td>4.7 (0.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IADL disability (IADL score &lt;5), n (%)</td>
<td>43</td>
<td>137 (8.4)</td>
<td>148 (15.6)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Statistical significance based on chi-square tests or t-tests, as appropriate. BMI, body mass index; K6, Kessler 6 psychological distress scale; MoCA-J, Japanese version of the Montreal Cognitive Assessment; IADL, instrumental activities of daily living.

Note: Data are represented as mean (SD) or n (%).
<table>
<thead>
<tr>
<th></th>
<th>Odds ratio (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model 1&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>ST per 1-SD increment</td>
<td>1.53* (1.25-1.87)</td>
</tr>
<tr>
<td>BST per 1-SD increment</td>
<td>0.74* (0.62-0.89)</td>
</tr>
</tbody>
</table>

Note: ST and BST were estimated by using the 90-minutes non-wear criterion. 1-SD for ST and BST are 106.8 minutes/day and 11.7 times/day. ST and BST were adjusted for wear time using the residual method prior to standardization. * Significant at p <0.05.<br>

<sup>a</sup> Model 1 adjusted for sex and age. <sup>b</sup> Model 2 adjusted for other confounding factors (years of education, body mass index, living status, multimorbidity, stair climbing difficulty, score of Japanese version of the Kessler 6 psychological distress scale, self-rated health, score of Japanese version of the Montreal Cognitive Assessment, and smoking habit) plus factors in Model 1 as covariates. <sup>c</sup> Model 3 adjusted for moderate-to-vigorous physical activity plus factors in Model 2 as a covariate. <sup>d</sup> Model 4 adjusted for factors in Model 3 plus BST or ST, appropriately. ST, sedentary time (adjusted for wear time); BST, breaks in sedentary time (adjusted for wear time); IADL, instrumental activities of daily living; SD, standard deviation.
Chapter 4. Association between tri-axial accelerometer-determined daily physical activity and cognitive function: a longitudinal population-based cohort study (Study 3)
1. Introduction

The percentage of the population aged 65 years old and over in Japan was 23.0%, which was the highest in the world in 2010 (Statistics Bureau of Japan, 2011). By 2035, 33.4% of the total population will be 65 years old and over. In other words, one in three people will be older adult in Japan in 2035 (National Institute of Population and Social Security Research, 2012). The rapid trend of population aging is accompanied by the increasing prevalence of dementia in Japan (Asada et al., 2013). Dementia, even mild cognitive impairment, increases disability and decreases quality of life (Leroi et al., 2012), it is anticipated that cognitive impairment or dementia will pose huge challenges to public health and care systems in Japan. Therefore, it is crucial to identify modifiable risk factors that are potentially associated with dementia and healthy cognition aging.

An increasing number of the literature highlights the potential benefits of PA on the cognitive function among older adults (Brown et al., 2013; Verghese et al., 2003; Weuve et al., 2004). Nevertheless, there is no consistent conclusion about the relationship between PA and cognitive decline (Sturman et al., 2005). To date, the majority of the evidence generated in this area has derived from estimates of physical activities from subjective measurement such as questionnaire and behavioral log (Verghese et al., 2003; Weuve et al., 2004). The use of questionnaires is potentially
subject to response bias, e.g. imprecise recall or misunderstanding, particularly in older adults (Kowalski et al., 2012; Taraldsen et al., 2012). Furthermore, questionnaires tend not to include LPA which is the common PA in older adults, while such activity might be important to the health outcomes in older adults (Buman et al., 2010).

Therefore, the lack of valid and precise instruments for assessing PA has been a serious limiting factor in this important area of research. To address this issue, accurate assessment of PA is necessary in order to estimate the strength of the association between PA and cognitive function. A tri-axial accelerometer is a simple but accurate tool to assess daily levels and patterns of physical activities under free-living conditions (Kumagai et al., 2015; Ohkawara et al., 2011). It offers an objective means for capturing daily PA patterns and levels of older adults and is not prone to response or recall biases.

Recently, Buchman et al. (2012) examined the association between daily PA, measured by accelerometers, and the incidence of Alzheimer disease. Results of this study showed that a higher level of total daily PA was associated with decreased risk of Alzheimer disease. However, knowledge regarding the association between PA and cognitive decline is scarce. In addition, a cognitive decline does not necessarily result in dementia or Alzheimer disease, and cognitive decline can be present up to 20 year prior to a dementia diagnosis (Kåreholt et al., 2011). For this reason, further study is still
needed to identify the effect of objective measured PA on age-associated cognitive
decline in older adults, which would help the primary prevention of subsequent
cognitive impairment and dementia.

The purpose of this study is therefore to examine whether objectively measured of
PA using a tri-axial accelerometer is associated with subsequent cognitive function in a
relative large sample of community-dwelling older adults without evidence of dementia.

2. Method

2-1. Participants

The data used in the present study were derived from the SGS, which is an ongoing
community-based prospective study in a local town, Sasaguri, established in 2011.
Method is described in detail elsewhere (Narazaki et al., 2013). Briefly, the primary aim
of this study was to explore modifiable lifestyle factors causing older adults to require
nursing care. Potential participants of the study were all residents of the town, who were
aged 65 years or older and not certified as individuals requiring nursing care by the
town in January 2011 (n=4,979). 66 subjects were excluded due to being dead or
moving out by the onset of the study. All remaining subjects (n=4,913) were invited to
participate in the study by letter. In total, 53.5% of those invited agreed to take part in
SGS-1(n=2,629) which was performed from May to August in 2011.

Of these who participated in the baseline survey, 1,060 participated in the first follow-up survey (SGS-2) 2 years later from May to July in 2013. Among the 1,060 participants, we excluded those who (1) had no information on MoCA-J and Mini-Mental State Examination (MMSE) at baseline(n=123); (2) had no valid data on PA at baseline(n=132); (2) were classed as probable dementia (MMSE score <24) or with self-reported histories of Parkinson’s disease and dementia at baseline (n=32); (3) needed nursing care or assistance at baseline (n=4); (4) were with missing variables of interest such as age, years of education (n=35). Finally, we excluded participants with no follow-up MoCA-J score (n=62). Thus, the remaining 672 participants were in the present analysis.

All the participants signed an informed consent form approved by the Institutional Review Board of Institute of Health Science, Kyushu University.

2-2. Cognitive function measures

Two cognitive function tests, the MoCA-J and MMSE, were administered by trained research assistants at baseline and 2 years later. Both MoCA-J and MMSE scores may range from 0-30 with higher scores indicating better cognitive function. One point was added to the total score of the cognitive tests if an individual had 12
years or fewer of formal education for the MoCA-J (Fujiwara et al., 2010).

2-3. PA measures

Total daily PA is measured by a tri-axial accelerometer (HJA-350IT; Active style Pro, Omron Healthcare Co., Ltd., Inc., Kyoto, Japan). The accelerometer has been showed to be accurate and feasible for estimation the intensity of various physical activities such as life-style PA under free-living conditions (Kumagai et al., 2015; Ohkawara et al., 2011; Oshima et al., 2010). Participants were ask to wear the accelerometer on their waist for up to 7 days and to remove the accelerometer only before going to bed and water activities. Data were collected in 1-minute epochs. Non-wearing time was defined as at least 60 consecutive minutes of zero activity intensity counts (zero counts, less than intensity of 1.0 METs). Total PA was the sum of all activity with an energy expenditure >1.5 METs during the day. Data for participants with at least 4 days with ≥10 hours per day of valid wear time were included in the analysis.

2-4. Covariates measures

Baseline characteristics such as demographic, health and other information were obtained from questionnaires. Education was assessed as the number of years of formal education. Body mass (kg) and height (m) were measured using conventional scales, and BMI was calculated by dividing the body mass by height squared (kg/m²).
Economic status was assessed by a subjective rating scale (Painful, somewhat painful, somewhat complacent, and complacent). Current smoking, current drinking and history of disease (Hypertension, heart disease, depression and diastolic mellitus) were self-reported in the questionnaires. Five physical fitness indices, hand-grip strength, leg strength, gait speed, open-eyed one-leg standing time, and five-time-sit-to-stand time, are objectively measured with conventional methods. IADL was assessed by using the first 5 questions of Instrumental Self-Maintenance of TMIG-IC (Koyano et al., 1991). Distress was assessed by using the K6 in the standard procedure (Furukawa et al., 2008).

2.5. Statistical analyses

Participant characteristics and cognitive test scores were summarized using means for continuous variables and percent for categorical variables. Differences in characteristics between baseline and follow-up were tested using Wilcoxon rank-sum test for continuous variables. The chi-square test was conducted to compare categorical variables. The Wilcoxon rank-sum test was also performed to assess the difference in age, years of education, MoCA-J score and total PA between the participants of the present study and the rest of participants of SGS-1 who have valid relevant data. First, we test the interaction between total PA and sex, age, years of education on MoCA-J.
score. No interactions were found (p for interaction ranged from 0.56 to 0.92). Therefore, all subsequent analyses were performed for the total sample. Multiple linear regression models were used to assess that whether baseline PA level was associated with subsequent MoCA-J scores over the 2 years follow-up. The basic model (model 1) adjusted for age, sex, education, BMI, wearing time and baseline MoCA-J score. Next, we added terms for potential confounding variables including economic status, current smoking, current drinking, participation in hoppy, physical functions, functional capacity (IADL), distress, and vascular-related diseases (hypertension, diabetes mellitus, heart disease and stroke) in the basic model (model 2). All statistical analyses were conducted using SAS version 9.2 (SAS Institute Inc., Cary, N.C., USA).

3. Results

Overall, there were 672 participants (percentage of men, 39.9%) completed both the baseline and follow-up survey (Table 5). The mean age of the participants at baseline was 72.3 years (SD, 5.5); mean education was 11.4 years (SD, 2.6). Total daily PA ranged from 4.3 to 27.6 METs-hour/day (mean, 14.9; SD, 4.5). The mean MoCA-J score was 24.0 points (SD, 3.2) at baseline.

The participants of the present study at baseline differed from the rest of the subjects
in terms of sex (p <0.05), age (p < 0.0001) and years of formal education (p <0.0001). The mean MoCA-J score of participant in present study was higher than the rest participants of SGS-1 who took part in the MoCA-J test (p<0.0001). Furthermore, total PA was also different between the participants of the present study and the rest of the participants of the SGS-1 who had valid accelerometer data (p<0.001) (Table 6).
Table 5. Characteristics of participants at baseline and follow-up (n=672)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Follow-up</th>
<th>Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>268(39.9)</td>
<td>268(39.9)</td>
<td>-</td>
</tr>
<tr>
<td>Age, years</td>
<td>72.3±5.5</td>
<td>74.3±5.5</td>
<td>2.0±0**</td>
</tr>
<tr>
<td>Formal education, year</td>
<td>11.4±2.6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.24±2.79</td>
<td>23.21±2.84</td>
<td>-0.05±1.11</td>
</tr>
<tr>
<td>Hand grip strength, kg</td>
<td>27.89±8.00</td>
<td>26.77±7.80</td>
<td>-1.16±3.05**</td>
</tr>
<tr>
<td>Knee extension strength, kg</td>
<td>26.90±9.99</td>
<td>28.72±10.89</td>
<td>1.71±7.22**</td>
</tr>
<tr>
<td>5-m gait speed, m/sec</td>
<td>1.81±0.43</td>
<td>1.78±0.44</td>
<td>-0.03±0.41**</td>
</tr>
<tr>
<td>One leg standing time, sec</td>
<td>69.54±47.43</td>
<td>65.30±47.34</td>
<td>-4.26±34.52**</td>
</tr>
<tr>
<td>5-times sit-to-stand rate, rep/sec</td>
<td>0.63±0.19</td>
<td>0.66±0.20</td>
<td>0.03±0.18*</td>
</tr>
<tr>
<td>IADL, point</td>
<td>4.9±0.3</td>
<td>4.9±0.3</td>
<td>0.0±0.3</td>
</tr>
<tr>
<td>Distress, point</td>
<td>2.9±2.9</td>
<td>2.7±3.0</td>
<td>-0.2±2.8*</td>
</tr>
<tr>
<td>Having hobby, n (%)</td>
<td>587(87.4)</td>
<td>630(93.8)</td>
<td>43(6.4)</td>
</tr>
<tr>
<td>Current drinker, n (%)</td>
<td>303(45.1)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>47(7.0)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Economic status, in (relatively)</td>
<td>386(57.4)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>249(37.1)</td>
<td>275(40.9)</td>
<td>26(3.9)</td>
</tr>
<tr>
<td>Stroke, n (%)</td>
<td>19(2.8)</td>
<td>22(3.3)</td>
<td>3(0.4)</td>
</tr>
<tr>
<td>Heart disease, n (%)</td>
<td>79(11.8)</td>
<td>81(12.1)</td>
<td>2(0.29)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>84(12.5)</td>
<td>93(13.8)</td>
<td>9(1.3)</td>
</tr>
<tr>
<td>Depression, n (%)</td>
<td>5(0.7)</td>
<td>4(0.6)</td>
<td>-1(0.1)</td>
</tr>
<tr>
<td>Regular exercise</td>
<td>434(64.6)</td>
<td>489(73.5)</td>
<td>55(9.0)</td>
</tr>
<tr>
<td>Accelerometer wear time, min/d</td>
<td>838.9±97.1</td>
<td>848.2±107.1</td>
<td>8.5±94.1*</td>
</tr>
<tr>
<td>Total PA, METS・h/d</td>
<td>14.9±4.5</td>
<td>14.6±4.6</td>
<td>-0.3±3.0*</td>
</tr>
<tr>
<td>MMSE score, point</td>
<td>28.3±1.6</td>
<td>28.2±1.8</td>
<td>-0.0±1.8</td>
</tr>
<tr>
<td>MoCA-J score, point</td>
<td>24.0±3.2</td>
<td>24.4±3.4</td>
<td>0.4±2.8**</td>
</tr>
</tbody>
</table>

Note: Data are represented as mean ± SD or n (%). * p value<0.05; ** p value<0.001. BMI, body mass index; IADL, instrumental activity of daily living; METs, metabolic equivalent of tasks; MMSE, Mini-Mental State Examination; MoCA-J, Japanese version of Montreal Cognitive Assessment.
Table 6. Differences in characteristics at baseline between participants and those who were excluded or declined to participate in the follow-up survey

<table>
<thead>
<tr>
<th></th>
<th>Participants</th>
<th>Non-participants</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>268 (39.9)</td>
<td>879 (44.9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Age, years</td>
<td>72.3±5.5</td>
<td>73.9±6.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Formal education, year</td>
<td>11.4±2.6</td>
<td>10.9±2.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total PA, METS • h/d</td>
<td>14.9±4.5</td>
<td>14.0±4.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MoCA-J score, point</td>
<td>24.0±3.2</td>
<td>21.9±4.0</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Note:* Data are represented as mean ± SD or n (%). METs, metabolic equivalents; MoCA-J, Japanese version of Montreal Cognitive Assessment.
Figure 5. Change in MoCA-J score over 2 years (n=672).

Note: Value of change was calculated by subtracting baseline MoCA-J score from follow-up MoCA-J score. A negative value means a decrease in MoCA-J score during the follow-up. MoCA-J, Japanese version of Montreal Cognitive Assessment.
Figure 5 showed the distributions of changes of MoCA-J score over 2 years. The mean of change in MoCA-J score was 0.4 (rang, -8 to 9 points). During the 2 years follow-up, the mean MoCA-J score significantly increased up to 24.4 points (SD,3.4 ) (p<0.001). On the other hand, the total PA significantly declined from baseline to follow-up by 0.3 METs-hour/day (p<0.05). Physical performance such as hand grip strength, one leg standing time and gait speed deteriorated over the 2 years follow-up, but not in terms of 5-times sit-to-stand rate and leg strength (Table 5). Additional characteristics were also included in Table 5.

There was no linear relationship between total PA and follow-up MoCA-J score in the multiple regression analysis in both basic model (regression coefficient, -0.02; 95% CI, -0.07 to 0.03; p=0.50) and in the fully adjusted model (regression coefficient, -0.04; 95% CI, -0.10 to 0.01; p=0.12) (Table 7).
### Table 7. Association of baseline PA and follow-up MoCA-J score

<table>
<thead>
<tr>
<th>Model</th>
<th>Regression coefficient β (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1 a</td>
<td>-0.02 (-0.07 to 0.03)</td>
<td>0.50</td>
</tr>
<tr>
<td>Model 2 b</td>
<td>-0.04 (-0.10 to 0.01)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Note: a Adjusted for MoCA-J score at baseline, sex, age, body mass index, years of education and accelerometer wear time. b Also adjusted for physical performance, instrumental activity of daily living, distress, having hobby, drinking and smoking habit, economic status, and current medical history. MoCA-J, Japanese version of Montreal Cognitive Assessment.
4. Discussion

In this longitudinal study, we examined the association between the daily PA and cognitive function in community-dwelling relatively healthy older adults. The results of the present study indicate that there is no linear relationship between total PA at baseline and follow-up cognitive function over 2 years in this cohort.

Previous studies have showed the protective effect of PA evaluated by questionnaire on cognitive function among the older adults (Verghese et al., 2003; Weuve et al., 2004). For example, Weuve et al. (2004) observed higher levels of PA, including walking, were associated with better cognitive performance. However, in the present study, PA objectively measured by accelerometers was not associated with cognitive performance. One possible explanation for the inconsistent findings is the reliability of PA data. Because the majority of previous studies in this area have included a subjective measure of PA, which may be affected by recall bias and has restricted the type of activities that sampled and may potentially distort relationships between PA and cognitive function. In contrast, accelerometer provides objectively measured of daily levels of physical activities that capture various physical activities under free-living conditions. Nevertheless, a detailed PA questionnaire could also be an informative source of information of different dimensions of PA such as frequency, type of PA (Lee, 2009).
Therefore, combining objective measured PA with questionnaires would likely provide future studies with a broad pattern of PA for the analysis of the association between PA and cognition.

In the present study, participants who involved in the follow-up survey had a younger age, higher years of education, higher baseline MoCA-J score and higher level of PA than those who did not participate in the follow-up survey (Table 6). In addition, given our exclusion criteria, individuals with probable dementia (MMSE score <24) or with self-reported histories of Parkinson’s disease and dementia at baseline were excluded, as well as those requiring nursing care or assistance at baseline. Regarding to the cognitive performance, the mean MoCA-J score significantly increased 0.42 points over 2 years (Table 5). Furthermore, physical performance such as leg strength and 5-times sit-to-stand rate did not decline during the follow-up (Table 5). Therefore, it is possible that no significant linear relationship between total PA and cognitive performance observed in our study is explained by relatively healthy status of the population.

It is also possible that PA may prevent cognitive decline but not during a short period in otherwise high functioning older adults. This is plausible if PA induced effects are associated with long-term protective benefits. Furthermore, considering the observable increase in cognitive performance over 2 years, the finding from the present study
emphasizes the importance of a longer follow-up period.

The main strength of the present study is the use of an accurate, objectively measured PA to examine relationship between total daily PA and cognitive function in a prospective cohort. In addition, with a relatively large well-characterized cohort, we are able to control for a wide range of potential confounding variables.

5. Conclusion

In summary, although PA have been shown favorable effect on cognitive health in older population, no linear relationship between total PA at baseline and follow-up cognitive function was observed over a follow-up of 2 years in this cohort. Considering our findings, future studies may be needed to more thoroughly assess the PA and normal cognitive aging with a longer follow-up period. Given that the SGS is ongoing prospective study, we are going to keep following the present participants to determine whether PA reduce the risk of cognitive decline, as well as the incidence of dementia for future efforts.
Chapter 5. Overall discussion and conclusion
The primary purpose of this doctoral thesis was to extend our knowledge regarding accelerometer-determined daily levels of PA and SED in community-dwelling older adults and then to investigate their associations with disability and cognitive function. Accordingly, the present thesis had three specific objectives as follows: (1) to objectively assess daily PA and SED in community-dwelling older adults, using tri-axial accelerometers (Study 1); (2) to examine the association between accelerometer-determined SED and IADL disability in community-dwelling older adults (Study 2); (3) to examine the association of accelerometer-determined PA and cognitive function in community-dwelling older adults (Study 3).

The first study described a detailed accelerometer-derived PA and SED levels in a relatively large population-based cohort of older Japanese adults, which is a population of particular public health interest given the Japanese society undergoing the world’s fastest aging with the highest life expectancy. Overall, the results from this study showed a high level of SED and low level of PA in the Japanese older population. This study also demonstrated that the levels of PA and SED differed by sex, age, and BMI. In contrast with previous observations in western populations, women were more active compared with men, providing unique insight into the current levels of PA and SED in this population. In fact, women spent more time in LPA and MVPA compared with men,
while men spent more time being sedentary. Data presented in this study fill a notable knowledge gap concerning objectively measured daily levels of PA and SED and will enable further investigation how these behaviors are related to health outcomes in this unique population.

The second study demonstrated that shorter time spent in SED and more BST were associated with lower risk of IADL disability, after adjusting known confounding factors and MVPA. In addition, the association between SED and IADL disability was independent of BST, and vice versa. These findings suggest not only total SED but also the patterns of SED may be independent associated health outcomes in older adults.

The third study was conducted to examine the longitudinal association between accelerometer-determined total PA and cognitive function in community-dwelling older adults free from apparent cognitive problems. Total PA was found to decrease significantly from baseline to follow-up, whereas cognitive function measured by MoCA-J appeared somewhat improved. In addition, no significant linear association between total PA and cognitive function was observed over a follow-up of two years. These findings indicated a longer follow-up period may be needed to clarify the relationship between PA and normal cognitive aging.

Findings from this thesis have several public health implications. First, objectively
measured PA and SED using accelerometer reveals Japanese older adults engage sparingly in MVPA and accumulated tremendous time being sedentary. Given the numerous health benefits of PA and SED emerged as a distinct risk factor for health, there is a great need for effective interventions targeting both behaviors. Second, the independent association of ST with IADL disability observed in the second study supports recent findings that sedentary behavior is a distinct health risk factor from the absence of MVPA in older adults and highlights the need of promotion of reduction of ST to avoid too much sitting even in those who have met the PA guideline of 30 minutes MVPA per day. Third, findings from the second study also provide novel evidence that not only total SED but also the manner in which it is accumulated may contribute the maintenance of functional capacity in older adults. As beneficial association were observed with BST that were relatively short in duration suggesting regularly break up or interrupt prolonged sedentary time may be feasible to implement in real-life setting in older adults, particularly in physically inactive individuals. Finally, results from the third study reveal that cognitive function appears stable in relatively functional older adults, highlighting the need for longer follow-up periods when investigating the protective effects of PA on cognitive function in non-demented population.

Despite the implications mentioned above, further studies using accelerometers is
needed to confirm and extend the present findings for better understanding the
dose-response relationships between PA, SED and health outcomes and informing
public health strategies related to PA and SED in older population. Specifically, future
study should assess PA and SED objectively using a nationally representative population
and establish age- and sex-specific reference values. Future studies should also explore
the associations of these objectively measured PA and SED with other health conditions
and the incidence of hard clinical endpoints (e.g., all-cause mortality, dementia) to
facilitate development of guidelines related to PA and SED in this population.
Furthermore, recent availability of data processing technique with accelerometer allows
for better characterizing patterns of PA and SED, such as frequency and duration of
bouts or intervals in different intensity activities. Future studies should also examine the
associations of these patterns of PA and SED with health outcomes (e.g. dose
comparable volumes of sporadic MVPA and longer bout MVPA influence health
outcomes to a similar magnitude?), which will be useful to inform lifestyle
interventions.

In conclusion, this doctoral thesis reveals that Japanese older adults spent majority of
the day being sedentary and accumulated few minutes of MVPA, and confirms that
SED is a distinct concept from insufficient MVPA and has independent effects on
health outcomes in older adults. These findings highlights the need of reducing overall
time spent in SED in community-dwelling older adults to optimize their health, beyond
encouraging PA. In addition, it also suggests breaking up prolonged sedentary time
may be beneficial for the maintenance of functional capacity in older adults. Although
no significant association between accelerometer-determined PA and cognitive
function was observed, the doctoral thesis has shown the feasibility and utility of the
accelerometer in longitudinal, large-scale epidemiology studies. Further studies will be
performed investigate the associations of these objectively measured behaviors with
other health conditions and the incidence of hard clinical endpoints (e.g., dementia,
all-cause mortality) to facilitate development of guidelines related to PA and SED in
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