Regional Cerebral Glucose Metabolism and Gait Speed in Healthy Community-Dwelling Older Women

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Background. The objective of this study was to investigate the relationship between normalized regional cerebral metabolic rates of glucose (normalized-rCMRglc) and gait function in physically and mentally high-functioning older women.

Methods. One hundred eighty-two community-dwelling older women (mean age [SD], 69.4 [6.6] years) without disability in instrumental activities of daily living and without mobility limitations underwent positron emission tomography with 18F-fluorodeoxyglucose at rest to assess brain activity associated with gait function. We measured normalized-rCMRglc in 16 regions of interest. Within 6 months of the positron emission tomography with 18F-fluorodeoxyglucose scan, gait speed, step length, and step frequency both at comfortable and maximum paces were measured as indices of gait function. Associations between normalized-rCMRglc and gait indices were examined with multiple linear regression analyses adjusted for demographic characteristics, including age, height, body weight, blood pressure, past illness, and education.

Results. Slower maximum gait speed even in the range of individual difference was associated with lower normalized-rCMRglc in the prefrontal, posterior cingulate, and parietal cortices. Lower step frequency at the maximum pace was also associated with lower normalized-rCMRglc in these regions. However, there was no significant association between step length at the maximum pace and normalized-rCMRglc or between all gait variables at a comfortable pace and normalized-rCMRglc.

Conclusions. The normalized-rCMRglc values in specific regions were associated with individual differences in gait function, even in healthy older women. These regions of the cerebrum could play an important role in gait control. Understanding the cerebral glucose metabolism in these brain regions may enable early detection of mobility limitation.

Key Words: Gait speed—Brain aging—Cerebral metabolic activity—FDG-PET—Older adults.

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Maintaining gait function is essential for older adults to independently undertake daily activities. Deterioration of gait function is an important risk factor for falls, cognitive impairment, institutionalization, and death (1–5), especially in older women who are predisposed to some mobility limitations and frailty (6). As there tends to be vast individual differences in the impact of aging on physical abilities (7), low gait performance without any mobility limitations is believed to be due to individual variation in healthy older adults that may lead to severe issues in the future. Therefore, understanding the underlying mechanism of age-related deterioration of gait function, including individual variation, may enable us to detect the risk of mobility limitation at an earlier stage.

Recently, strong evidence of the relationship between age-related gait dysfunction and cerebral neurological (central nervous system) changes has been observed (8). Some studies have shown that diffused brain magnetic resonance imaging (MRI) abnormalities such as white matter hyperintensity are associated with gait dysfunction (9–11). Furthermore, other recent studies have indicated a relationship between specific regional brain volume and gait function (12–15). These findings are a valuable contribution to understanding the underlying mechanisms of age-related mobility limitation. However, although brain volume is considered to be correlated with cerebral glucose metabolism and cerebral blood flow as indicators of functional brain activity (16), previous studies have suggested that these
do not always correlate simultaneously in older adults, for example, in patients with Alzheimer disease (17,18). It is therefore possible that evaluating cerebral glucose metabolism levels, rather than measuring brain atrophy, will lead to early detection in older adults at risk of deteriorating gait function.

A previous study using single-photon emission computed tomography to measure regional cerebral blood flow reported that older adults with gait disturbance secondary to age-related white matter changes exhibited lower activation of the supplementary motor area, thalamus, and basal ganglia during treadmill walking than those without any gait disturbance (19). Furthermore, in a study by using positron emission tomography with 18F-fluorodeoxyglucose (FDG-PET) to measure cerebral glucose metabolism, Shimada and colleagues (20) found that older adults who had high step length variability showed significant deactivations in the frontal lobe and the inferior temporal gyrus during treadmill walking. However, it is still unclear whether there is a close relationship between deterioration of gait function and functional brain activity considering that treadmill walking is different from walking in a natural environment (20). It is also unclear whether lower gait performance without any mobility limitations (differences resulting from individual variations) is associated with functional brain activity in healthy older adults.

In this study, we investigated the relationship between regional cerebral glucose metabolic values and indices of gait function (4,21,22) in physically and mentally high-functioning older women without any mobility limitations. By using FDG-PET, we measured the regional cerebral glucose metabolic values in 16 regions related to gait and motor control (Figure 1), gait speed, step length, and step frequency as indices of gait function.

**Methods**

**Participants**

The participants recruited were community-dwelling older adults from our volunteer database (recruited by telephone or newsletter from an urban area between 2004 and 2011), of whom 230 agreed to participate in the study. Participants traveled to the Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology, and underwent cognitive function assessments (Mini-Mental State Examination) as well as MRI and FDG-PET examinations in a fasting state of at least 5 hours. Gait function was assessed within 6 months of the FDG-PET.

The exclusion criteria were as follows: (i) instrumental activities of daily living-associated problems identified by the TMIG-Index of Competence (23) and mobility limitations identified by a questionnaire relating to stair climbing and walking (24); (ii) severe conditions or injuries (eg, stroke, heart disease, and injury-related falls) within 3 months before the study; (iii) history of cerebrovascular disorder; (iv) problems with motor function (use of a walking aid such as a cane); (v) mental disorders and cognitive impairment (Mini-Mental State Examination score <27); and (vi) abnormal anatomical MRI (eg, high cortical atrophy or white matter hyperintensity, which are defined as >grade 1 on the Fazekas scale) findings diagnosed by experienced neuroradiologists. In total, 182 older women (mean age [SD], 69.4 [6.6] years) were included in the study. Written informed consent was obtained from all participants before examination. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki (1983), and the research protocol was approved by the Ethics Committee of the Tokyo Metropolitan Institute of Gerontology.
Measurements

MRI and PET protocol.—The three dimensional MRI images comprised T1-weighted contrast and screening T2-weighted scans that were obtained by using a 1.5-T Sigma Excite scanner (GE, Milwaukee, WI). After obtaining the MRI scan, FDG-PET images, which were used to evaluate cerebral glucose metabolism, were obtained by using a PET scanner (SET 2400W; Shimadzu, Kyoto, Japan) in the three dimensional mode (image resolution: transverse full width at half-maximum = 4.4 mm, and axial full width at half-maximum = 6.5 mm). Forty-five minutes after the intravenous injection of FDG (approximately 150 MBq), a 6-minute emission scan was used to create images with the following parameters: matrix size was 128 × 128 (transverse section) × 50, and voxel size was 2 × 2 × 3.125 mm. Attenuation was corrected with a transmission scan by using a 68Ga/68Ge source. During the tracer accumulation phase, the participants remained supine, quiet, and motionless in a dimly lit, quiet room with their eyes open and their ears unplugged. A total of 1–2 mL of venous blood was drawn twice, immediately before the intravenous FDG injection and 30 minutes after the injection, and the plasma glucose concentration was measured.

Image Processing

All FDG images were spatially normalized and resampled (XYZ matrix 79 × 95 × 80 and voxel size 2 × 2 × 2 mm) with the FDG template created from the FDG images of 15 physically and psychiatrically healthy subjects by using SPM8 (Wellcome Trust Centre for Neuroimaging, London, UK). An experienced neurologist (K.I.) placed a template of regions of interests (ROIs) consisting of a set of circles 10 mm in diameter on the average FDG image in the standard anatomical space, by using Dr. View software (AJS, Tokyo, Japan). The ROIs were defined as regions known from the results of previous studies to be associated with gait and motor control (Figure 1). A total of 32 ROIs were placed and then bilaterally averaged to 16 ROIs. The regional cerebral glucose metabolic values were obtained for each subject after adjusting the standard ROI set on individual FDG images by another analyst (R.S.) to prevent misalignment.

Cerebral glucose metabolism is affected by anatomical differences (eg, whole brain volume, brain shape, and body size). Therefore, the regional cerebral glucose metabolic values were normalized in reference to the cerebellar glucose metabolic value (formula: regional cerebral glucose metabolic value for each region/cerebellar glucose metabolic value × 100) because this methodology has been widely adopted for many studies, considering that glucose metabolism in the cerebellum is relatively unaffected either by normal or pathological aging (eg, Alzheimer disease) (25–27). However, it is possible that the cerebellar glucose metabolic value itself is associated with gait function (12,15). Therefore, first, we examined the relationships between each of the gait variables and cerebellum glucose metabolism. In this case, the glucose metabolic value in the cerebellum was normalized in reference to the global cerebral glucose metabolic value as it has been widely used in other studies (26,27) (formula: cerebellar glucose metabolic value/global cerebral glucose metabolic value [excluded cerebellum] × 100). In the present study, these normalized values were defined as normalized regional cerebral metabolic rates of glucose (normalized-rCMRglc). This prior analysis showed that there were no relationships between normalized-rCMRglc in cerebellum and all gait variables even without adjusting for covariates. (Tables 2 and 3).

Gait Variables

Within before and after 3 months of examining the FDG-PET, we measured participants’ gait speed, step length, and step frequency (cadence) at comfortable and maximum paces as indices of gait ability (4). To test the gait speed, a trained tester asked the participants to walk once along an 11-m straight walkway on a flat surface at their comfortable pace (comfortable gait speed [CGS]) and then to walk twice along the walkway at their maximum pace (maximum gait speed [MGS]). Gait speed (m/min) was measured over a 5-m distance between marks 3 and 8 m from the start of the walkway. Simultaneously, two other testers measured the mean step length by marking heel points near the tape at 3 and 8 m and dividing the distance between the two heel points (in centimeters) by the number of steps required. Step frequency (steps/s) was defined as the number of steps per 5-m walking distance divided by the 5-m walking time (noted previously).

Covariates

All participants were interviewed by either a physician or a physical therapist to assess health-related characteristics that could be associated with gait function and FDG-PET abnormalities (covariates), which are listed as follows: demographic characteristics (age and education); anamnesis (hypertension, cardiac disease, and diabetes mellitus); and height, weight, and blood pressure. Participants with diabetes mellitus had good control and no peripheral neuropathy. All variables were assessed before the FDG-PET except for the height and weight, which were collected at the same time as the gait function measurements. In addition, we calculated the period (days) between the FDG-PET and the gait function assessments.

Statistical Analysis

To examine the relationships among age and gait variables, we performed a partial correlation analysis adjusted for height, which is believed to influence gait function. The relationships between each of the gait variables and...
normalized-rCMRglc were examined by using multiple linear regression analysis adjusted for demographic characteristics, anamnesis, height, weight, blood pressure, and the period between FDG-PET and the gait function assessments. Regression analysis was performed separately for each normalized-rCMRglc because their values were highly correlated with each other ($r > .5$). Thus, a Bonferroni correction for $p < .003$ was applied to avoid type 1 error ($p = .05/16$). All statistical analyses were performed by using a PC-compatible version of IBM SPSS Statistics, version 20.0 (SPSS Inc., Chicago, IL).

**Results**

Table 1 shows descriptive statistics for the covariates and gait variables. All results are shown as mean (standard deviation) and number (%). More than half of our participants (54.4%) were aged <70 years.

There were low correlation coefficients for CGS and age ($r = -.13, p = .09$) and for MGS and age ($r = -.16, p < .05$). The step length was significantly correlated with age (CGS, $r = -.29, p < .01$; MGS, $r = -.26, p < .01$), whereas step frequency was not (CGS, $r = - .05, p = .52$; MGS, $r = -.06, p = .42$). During CGS, both step length and step frequency were strongly correlated with gait speed ($r = .66, p < .01$; $r = .69, p < .01$). Moreover, the correlation coefficients between MGS and step length ($r = .38, p < .01$) and between MGS and step frequency ($r = .75, p < .01$) were also significant, with the MGS–step frequency correlation coefficient being significantly larger than the MGS–step length correlation coefficient ($p < .01$).

Table 2 shows the results of the multiple linear regression analysis of comfortable gait variables (speed, step length, and step frequency) and normalized-rCMRglc. No relationship was observed between normalized-rCMRglc and CGS at $p < .003$ even without adjusting for covariates. During CGS, no relationship was observed between normalized-rCMRglc or step length and step frequency.

For the maximum gait (Table 3), slower MGS was associated with lower normalized-rCMRglc in the prefrontal, posterior cingulate, and parietal cortices, independent of significant cognitive decline and other health-related factors, whereas CGS was poorly correlated with normalized-rCMRglc in physically and mentally high-functioning community-dwelling older women. During maximum gait, lower step frequency was related to lower normalized-rCMRglc. These results indicate that selective normalized-rCMRglc could be involved in the control of gait functions that require higher motor control, such as brisk walking. To the best of our knowledge, these results provide the first evidence of a relationship between cerebral glucose metabolism in the resting state and gait function in older adults. Understanding cerebral glucose metabolism in these brain regions may be useful for planning interventional strategies to prevent gait limitations.

As decreased normalized-rCMRglc may indicate reduced neural activity in the activated region, the results of the present study suggest that the prefrontal, posterior cingulate, and parietal cortices are cerebral regions (neural basis) that play an important role in gait control. The findings of the present study are at least partly consistent with those from previous studies that examined the relationship between age-related cerebral neurological change and gait function (12,14,20). Selective atrophy in the prefrontal cortex has been associated with slower gait (12,14). Similarly, a few studies have indicated that cerebral glucose metabolism in the prefrontal cortex is associated with a controlled gait (20). These findings suggest that the prefrontal cortex may control overall gait speed regulation (eg, balance and limb control). The posterior cingulate cortex is known as the brain region that has preferentially decreased cerebral glucose metabolism in the early stages of Alzheimer disease (28,29), and is strongly associated with cognitive function (30,31). Regional gray matter atrophy in the posterior cingulate cortex is also associated with freezing of gait in

**Discussion**

The key findings in this cross-sectional study were that slower MGS (believed to be due to individual variation) was associated with lower normalized-rCMRglc in the prefrontal, posterior cingulate, and parietal cortices, independent of significant cognitive decline and other health-related factors, whereas CGS was poorly correlated with normalized-rCMRglc in physically and mentally high-functioning community-dwelling older women. During maximum gait, lower step frequency was related to lower normalized-rCMRglc. These results indicate that selective normalized-rCMRglc could be involved in the control of gait functions that require higher motor control, such as brisk walking. To the best of our knowledge, these results provide the first evidence of a relationship between cerebral glucose metabolism in the resting state and gait function in older adults. Understanding cerebral glucose metabolism in these brain regions may be useful for planning interventional strategies to prevent gait limitations.

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Table 2. Results of Multiple Linear Regression Analysis of Variables of Participants While Walking at Comfortable Gait Speeds

<table>
<thead>
<tr>
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<th>Gait Speed</th>
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<tr>
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<td>β (95% CI)</td>
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<td>β (95% CI)</td>
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<td>β (95% CI)</td>
</tr>
<tr>
<td>Pons</td>
<td>.05 (−0.22, 0.44)</td>
<td>.04 (−0.26, 0.42)</td>
<td>.01 (−0.15, 0.17)</td>
<td>.002 (−0.16, 0.16)</td>
<td>.01 (−0.01, 0.01)</td>
<td>.003 (−0.01, 0.01)</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>−.04 (−0.41, 0.24)</td>
<td>−.04 (−0.43, 0.23)</td>
<td>−.08 (−0.25, 0.07)</td>
<td>−.09 (−0.26, 0.06)</td>
<td>−.07 (−0.01, 0.003)</td>
<td>−.06 (−0.01, 0.004)</td>
</tr>
<tr>
<td>Orbitofrontal cortex</td>
<td>−.09 (−0.44, 0.12)</td>
<td>−.11 (−0.49, 0.08)</td>
<td>−.12 (−0.25, 0.03)</td>
<td>−.11 (−0.25, 0.03)</td>
<td>−.08 (−0.01, 0.002)</td>
<td>−.11 (−0.01, 0.001)</td>
</tr>
<tr>
<td>Caudate nucleus</td>
<td>.01 (−0.18, 0.19)</td>
<td>−.03 (−0.23, 0.15)</td>
<td>−.01 (−0.09, 0.09)</td>
<td>−.03 (−0.11, 0.07)</td>
<td>−.06 (−0.01, 0.002)</td>
<td>−.09 (−0.01, 0.001)</td>
</tr>
<tr>
<td>Putamen</td>
<td>.01 (−0.19, 0.22)</td>
<td>−.02 (−0.24, 0.19)</td>
<td>.01 (−0.09, 0.11)</td>
<td>.001 (−0.10, 0.10)</td>
<td>−.06 (−0.01, 0.002)</td>
<td>−.09 (−0.01, 0.002)</td>
</tr>
<tr>
<td>Thalamus</td>
<td>.01 (−0.24, 0.29)</td>
<td>−.02 (−0.31, 0.24)</td>
<td>.06 (−0.07, 0.19)</td>
<td>.04 (−0.10, 0.16)</td>
<td>−.10 (−0.01, 0.002)</td>
<td>−.10 (−0.01, 0.002)</td>
</tr>
<tr>
<td>Precuneus</td>
<td>−.04 (−0.22, 0.13)</td>
<td>−.05 (−0.24, 0.12)</td>
<td>−.09 (−0.14, 0.03)</td>
<td>−.09 (−0.14, 0.03)</td>
<td>−.03 (−0.004, 0.003)</td>
<td>−.06 (−0.01, 0.002)</td>
</tr>
<tr>
<td>Temporal cortex</td>
<td>−.09 (−0.35, 0.09)</td>
<td>−.12 (−0.40, 0.05)</td>
<td>−.13 (−0.21, 0.01)</td>
<td>−.13 (−0.21, 0.003)</td>
<td>−.13 (−0.01, 0.001)</td>
<td>−.15 (−0.01, 0.001)</td>
</tr>
<tr>
<td>Prefrontal cortex</td>
<td>−.03 (−0.30, 0.19)</td>
<td>−.05 (−0.34, 0.17)</td>
<td>−.06 (−0.17, 0.07)</td>
<td>−.10 (−0.21, 0.04)</td>
<td>−.10 (−0.01, 0.002)</td>
<td>−.09 (−0.01, 0.002)</td>
</tr>
<tr>
<td>Dorsolateral prefrontal cortex</td>
<td>−.06 (−0.36, 0.15)</td>
<td>−.08 (−0.40, 0.11)</td>
<td>−.10 (−0.21, 0.04)</td>
<td>−.14 (−0.25, 0.001)</td>
<td>−.09 (−0.01, 0.002)</td>
<td>−.07 (−0.01, 0.002)</td>
</tr>
<tr>
<td>Primary sensorimotor cortex</td>
<td>−.01 (−0.26, 0.22)</td>
<td>−.05 (−0.34, 0.16)</td>
<td>−.13 (−0.23, 0.01)</td>
<td>−.17 (−0.26, −0.02)</td>
<td>−.02 (−0.01, 0.004)</td>
<td>−.03 (−0.01, 0.004)</td>
</tr>
<tr>
<td>Anterior cingulate cortex</td>
<td>−.05 (−0.36, 0.17)</td>
<td>−.09 (−0.43, 0.12)</td>
<td>−.10 (−0.22, 0.04)</td>
<td>−.13 (−0.25, 0.01)</td>
<td>−.10 (−0.01, 0.002)</td>
<td>−.10 (−0.01, 0.002)</td>
</tr>
<tr>
<td>Occipital cortex</td>
<td>−.11 (−0.32, 0.04)</td>
<td>−.12 (−0.34, 0.04)</td>
<td>−.14 (−0.18, −0.001)</td>
<td>−.12 (−0.17, 0.02)</td>
<td>−.11 (−0.01, 0.001)</td>
<td>−.13 (−0.01, 0.001)</td>
</tr>
<tr>
<td>Posterior cingulate cortex</td>
<td>−.03 (−0.22, 0.15)</td>
<td>−.04 (−0.25, 0.14)</td>
<td>−.04 (−0.15, 0.04)</td>
<td>−.10 (−0.16, 0.03)</td>
<td>−.04 (−0.01, 0.003)</td>
<td>−.05 (−0.01, 0.002)</td>
</tr>
<tr>
<td>Parietal cortex</td>
<td>−.07 (−0.37, 0.14)</td>
<td>−.09 (−0.42, 0.11)</td>
<td>−.11 (−0.22, 0.03)</td>
<td>−.12 (−0.24, 0.02)</td>
<td>−.10 (−0.01, 0.002)</td>
<td>−.12 (−0.01, 0.001)</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>.03 (−4.36, 6.62)</td>
<td>.06 (−3.45, 7.84)</td>
<td>.08 (−1.12, 4.24)</td>
<td>.10 (−0.78, 4.61)</td>
<td>.08 (−0.05, 0.16)</td>
<td>.09 (−0.04, 0.17)</td>
</tr>
</tbody>
</table>

Notes: CI = confidence interval; FDG-PET = positron emission tomography with 18F-fluorodeoxyglucose; Model 1 = adjusted for age; Model 2 = adjusted for demographic characteristics (age and education), anamnesis (hypertension, cardiac disease, and diabetes mellitus), height, weight, and blood pressure, and the time period between FDG-PET and the gait assessments.
Table 3. Results of Multiple Linear Regression Analysis of Variables of Participants While Walking at Maximum Gait Speeds

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</tr>
<tr>
<td>Pons</td>
<td>−0.03 (−0.64, 0.40)</td>
<td>−0.04 (−0.66, 0.40)</td>
<td>−0.03 (−0.24, 0.15)</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>0.09 (−0.19, 0.83)</td>
<td>0.10 (−0.18, 0.86)</td>
<td>0.04 (−0.19, 0.20)</td>
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<tr>
<td>Orbitofrontal cortex</td>
<td>0.14 (−0.04, 0.83)</td>
<td>0.13 (−0.06, 0.84)</td>
<td>0.04 (−0.11, 0.21)</td>
</tr>
<tr>
<td>Caudate nucleus</td>
<td>0.17 (0.04, 0.61)</td>
<td>0.14 (−0.02, 0.57)</td>
<td>0.08 (−0.05, 0.17)</td>
</tr>
<tr>
<td>Putamen</td>
<td>0.16 (0.03, 0.67)</td>
<td>0.14 (−0.03, 0.64)</td>
<td>0.07 (−0.06, 0.18)</td>
</tr>
<tr>
<td>Thalamus</td>
<td>0.02 (−0.35, 0.47)</td>
<td>−0.01 (−0.44, 0.41)</td>
<td>0.09 (−0.06, 0.25)</td>
</tr>
<tr>
<td>Prefrontal cortex</td>
<td>0.19 (0.08, 0.62)</td>
<td>0.19 (0.07, 0.63)</td>
<td>0.05 (−0.07, 0.14)</td>
</tr>
<tr>
<td>Temporal cortex</td>
<td>0.18 (0.09, 0.76)</td>
<td>0.17 (0.06, 0.76)</td>
<td>−0.01 (−0.14, 0.12)</td>
</tr>
<tr>
<td>Prefrontal cortex</td>
<td>0.22* (0.21, 0.97)</td>
<td>0.22* (0.20, 0.98)</td>
<td>0.10 (−0.04, 0.25)</td>
</tr>
<tr>
<td>Ventrolateral prefrontal cortex</td>
<td>0.19 (0.11, 0.88)</td>
<td>0.18 (0.08, 0.88)</td>
<td>0.03 (−0.12, 0.18)</td>
</tr>
<tr>
<td>Primary sensorimotor cortex</td>
<td>0.20 (0.14, 0.88)</td>
<td>0.18 (0.08, 0.86)</td>
<td>0.06 (−0.08, 0.20)</td>
</tr>
<tr>
<td>Anterior cingulate cortex</td>
<td>0.16 (0.04, 0.86)</td>
<td>0.15 (−0.01, 0.84)</td>
<td>0.07 (−0.09, 0.23)</td>
</tr>
<tr>
<td>Occipital cortex</td>
<td>0.16 (0.02, 0.59)</td>
<td>0.15 (−0.01, 0.59)</td>
<td>−0.001 (−0.11, 0.11)</td>
</tr>
<tr>
<td>Posterior cingulate cortex</td>
<td>0.22* (0.13, 0.70)</td>
<td>0.22* (0.13, 0.73)</td>
<td>0.04 (−0.08, 0.14)</td>
</tr>
<tr>
<td>Parietal cortex</td>
<td>0.24* (0.24, 1.02)</td>
<td>0.25* (0.26, 1.08)</td>
<td>0.07 (−0.08, 0.22)</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>−0.16 (−20.39, 0.39)</td>
<td>−0.15 (−20.16, 0.50)</td>
<td>−0.06 (−4.53, 1.92)</td>
</tr>
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Notes: CI = confidence interval; FDG-PET = positron emission tomography with 18F-fluorodeoxyglucose; Model 1 = adjusted for age; Model 2 = adjusted for demographic characteristics (age and education), anamnesis (hypertension, cardiac disease, and diabetes mellitus), height, weight, and blood pressure, and the time period between FDG-PET and the gait assessments.

*p < .003.
patients with Parkinson’s disease (32). This might indicate that the posterior cingulate cortex controls co-ordinated limb movement (ie, the ability for smooth alternative leg movement) because bilateral unco-ordinated gait and marked gait asymmetry also are associated with freezing of gait in patients with Parkinson’s disease (33). Considering the parietal cortex, a previous study showed that the right posterior superior parietal cortex is associated with balance difficulties (12), maybe because the posterior parietal cortex in the right hemisphere regulates visuospatial attention and balance (34,35). Our study with FDG-PET was not used to examine bilateral differences in the cerebrum. However, previous studies support our suggestion that the parietal cortex could support functions requiring balance, such as brisk walking. According to the data from previous studies and from our own results, slower gait may be associated with deterioration of the underlying neural circuits regarding gait control, such as the prefrontal, posterior cingulate, and parietal cortices.

Gait is thought of as an activity that requires high cognitive function (eg, executive, attention) as well as judgment of external and internal cues. Several studies have indicated that gait function is closely related to cognitive function (14,36–38). Rosano and colleagues (14) have indicated the possibility that a smaller volume of the prefrontal area may contribute to slower gait by decreasing cognitive function, such as slower information processing. As described previously, the posterior cingulate cortex, which was associated with gait speed in the present study, is also strongly associated with cognitive function (30,31). Furthermore, the prefrontal, posterior cingulate, and parietal cortices are known to be constitutive parts of the default mode network, which is a set of interactive subsystems used together during a passive task (39); several studies have shown that compared with older adults with normal cognitive ability, those with Alzheimer disease show an association with disruptions of the default mode network (40–42). These suggest that motor control and cognitive functions might share the same neural basis. Further longitudinal studies will be needed to understand the characteristics of cerebral glucose metabolism relating both of gait and cognitive dysfunction, and whether gait function requiring fine control of stepping movements could be controlled by fine-tuned activity of the default mode network.

Our study showed that the prefrontal, posterior cingulate, and parietal cortices were significantly associated with the step frequency, but not with the step length. As we age, both the step frequency and step length decline (43). Previous studies have indicated that during brisk walking at the same speed, older adults tend to have a faster step frequency, and young adults tend to have a longer step length (44). Our correlation analyses showed that the correlation between the MGS and step frequency was significantly stronger than that between the MGS and step length ($r = .75$ and $r = .38$, $p < .01$), whereas CGS was strongly correlated with both the step frequency and step length ($r = .69$ and $r = .66$, no significant difference). This observation implies that the physically and mentally high-functioning older women in this study could adopt the strategy of using a faster step frequency to boost their gait speed during brisk walking; the relationship between MGS and normalized-rCMRglc observed in this study strongly reflects differences in the ability to regulate step frequency (eg, motor control, rapid alternative leg movement) during brisk walking.

Contrary to the MGS findings, CGS was not related to normalized-rCMRglc in the present study. A possible explanation is that there were few differences in CGS among our participants because they all had very good physical ability. The participants in our study were 1.2 times faster than those in the study by Hageman and Blanke (45) (mean age, 66.8 years), and 1.7 times faster than those in the study by Rosano and colleagues (12) (mean age, 78.3 years). As noted, this observation indicates that our study participants had greater physical ability, but variations in the interpretation of the assessment instructions are also possible. That is, some participants might have walked faster than their actual comfortable pace during CGS assessments. The discrepancy between the findings of our study and those of previous studies that examined the relationship between CGS and cerebral neurological changes by using MRI (11–13) may be attributed to these factors. Further studies are required to assess the relationship between cerebral glucose metabolism and CGS in frail older adults.

Our study has several limitations. First, we did not examine the differences between cerebral glucose metabolism of the whole brain and of the two lobes. Examining relationships among brain regions that were not a focus of this study and bilateral differences in cerebral glucose metabolism and gait function could produce new findings about cerebral localization. Second, we analyzed only physically and mentally high-functioning older women in order to examine the relationship between cerebral glucose metabolism and gait function without any pronounced decline (differences due to individual variation). However, the strength of our study includes the finding that cerebral glucose metabolism in specific brain regions was associated with individual differences in gait function even in healthy older women, indicating the possibility of early detection of deterioration in gait function. Early detection of gait function deterioration by examining functional brain activity may contribute to the administration of preventive medicine (eg, interventions for long-term care and prevention), and would be significant for geriatric gerontology. The study will need to be repeated with a more diverse sample in terms of sex and mobility, and as a longitudinal study accounting for the previously mentioned limitations of the present study.

**Conclusion**

Our study provides preliminary evidence that lower normalized-rCMRglc in the prefrontal, posterior cingulate,
and parietal cortices is associated with slower gait speed and lower step frequency even in physically and mentally high-functioning older women without any mobility limitations, independent of significant cognitive decline and other health-related factors. It has been argued that these regions of the cerebrum play an important role in gait control. Understanding the cerebral glucose metabolism in these brain regions may enable early detection of mobility limitation.

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