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Research Article

Association Between Brain Volumes and Patterns of Physical Activity in Community-Dwelling Older Adults

Amal A. Wanigatunga, PhD, MPH,[1,2,*] Hang Wang, PhD, MHS,[2] Yang An, MS,[3] Eleanor M. Simonsick, PhD,[3] Qu Tian, PhD, MS,[3] Christos Davatzikos, PhD,[4] Jacek K. Urbanek, PhD,[5] Vadim Zipunnikov, PhD,[6] Adam P. Spira, PhD,[2,7] Luigi Ferrucci, MD, PhD,[3] Susan M. Resnick, PhD,[3] and Jennifer A. Schrack, PhD[1,2]

[1]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland. [2]Center on Aging and Health, Johns Hopkins University, Baltimore, Maryland. [3]Intramural Research Program, National Institute on Aging, Baltimore, Maryland. [4]Center for Biomedical Image Computing and Analytics, University of Pennsylvania, Philadelphia, Pennsylvania. [5]Division of Geriatric Medicine, Johns Hopkins University and Medical Institutions, Baltimore, Maryland. [6]Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland. [7]Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland.

*Address correspondence to: Amal A. Wanigatunga, PhD, MPH, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, E6040, Baltimore, MD 21205. E-mail: awaniga1@jhu.edu

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Abstract

Background: Larger brain volumes are often associated with more free-living physical activity (PA) in cognitively normal older adults. Yet, whether greater brain volumes are associated with more favorable (less fragmented) PA patterns, and whether this association is stronger than with total PA, remains unknown.

Methods: Brain magnetic resonance imaging and wrist-worn accelerometer data were collected in 301 participants (mean age = 77 [*SD* = 7] years, 59% women) enrolled in the Baltimore Longitudinal Study of Aging. Linear regression models were fit to examine whether brain volumes (cc) were cross-sectionally associated with: (a) total daily PA minutes and (b) activity fragmentation (mean number of PA bouts / total PA minutes × 100). Sensitivity analyses were conducted by adjusting for counterpart PA variables (eg, fragmentation covariate included in the PA minutes model).

Results: Greater white matter volumes in the parietal and temporal lobes were associated with higher daily PA minutes (2.6 [*SE* = 1.0] and 3.8 [0.9] min/day, respectively; $p < .009$ for both) after adjusting for demographics, behavioral factors, medical conditions, gait speed, apolipoprotein E e4 status, and intracranial volume. Greater temporal white matter volume was associated with lower fragmentation (–0.16% [0.05], $p = .003$). In sensitivity analyses, observed associations between brain volumes and daily PA minutes remained significant while associations with fragmentation no longer remained significant.

Conclusions: Our results suggest white matter brain structure in cognitively normal older adults is associated with the total amount of PA and, to a lesser extent, the PA accumulation patterns. More work is needed to elucidate the longitudinal relationship between brain structure and function and PA patterns with aging.

Keywords: Aging, Brain structure, Fragmentation, Total activity, White matter

With aging, the volume of brain gray and white matter declines, and the ventricles increase in size (1–4). Brain atrophy is associated with a higher risk of mild cognitive impairment and dementia, particularly Alzheimer's disease and related dementias (5,6). Efforts to mitigate and even prevent cognitive decline that results in dementia have focused largely on changing health behaviors such as increasing physical activity (7,8).

The relationship between physical activity and brain health may be bidirectional (8). A large body of evidence shows that increasing volitional physical activity may slow cognitive decline and protect

against brain atrophy (9), largely observed in the frontal, parietal, and temporal lobes (10). Possible biological mechanisms include brain-derived neurotrophic factor expression (11) and cardiovascular health through its role in supporting angiogenesis, neurogenesis, neuroplasticity, and synaptogenesis (12). Yet, little work has examined brain characteristics that influence total daily physical activity and its accumulation throughout the day (8). This is important because brain atrophy, low daily physical activity, and greater sedentary behavior are all associated with adverse health outcomes (13–15).

Upon reaching older ages, it is likely that brain structural integrity may influence the amount of physical activity in which older adults engage, as well as the way they cycle through states of physical activity and inactivity throughout the day (eg, "activity fragmentation"), which may be attributable to the perception of activity-related fatigue and limitations in physical function (16,17). Activity fragmentation can be operationalized using continuously collected physical activity data from wrist-worn accelerometers—portable, noninvasive devices that objectively measure daily physical activity over long periods of time. Activity fragmentation is more strongly associated with physical fatigability (18), low physical function and endurance (18), cancer history (19), and increased risk of mortality (20) than total daily physical activity. Moreover, activity fragmentation appears to occur before overall declines in physical activity and physical functioning (18) and may thus act as an early marker of adverse health conditions—such as accelerated brain atrophy—in older adults. Whether lower brain volumes (global or regional) are associated with higher activity fragmentation remains unexplored.

Using brain magnetic resonance imaging (MRI) and objectively measured physical activity from accelerometers, this study aimed to characterize the degree to which brain volumes are associated with physical activity in terms of both amount of physical activity and patterns of physical activity accumulated throughout the day in well-functioning and cognitively normal older adults. We hypothesized that higher brain volumes are associated with (a) higher total daily physical activity and (b) lower fragmentation of physical activity.

Method

Study Design and Population

Objective physical activity and brain MRI data were collected in the Baltimore Longitudinal Study of Aging (BLSA) between February 2015 and June 2018 (Supplementary Figure 1). The BLSA is an ongoing continuously enrolled cohort study primarily focused on studying normative aging in humans that is conducted by the National Institute on Aging's Intramural Research Program. Details of the BLSA and the enrollment criteria are published elsewhere (21). Briefly, the BLSA recruits persons aged 20 and older with no cognitive impairment, functional limitations, or major chronic disease (except hypertension or cancer within the past 10 years). Once enrolled, BLSA participants are followed up for life. Participants undergo comprehensive health, cognitive, and functional assessments during a 3-day stay at the NIA's Clinical Research Unit located at Harbor Hospital in Baltimore, Maryland. Visits are regularly scheduled every 1–4 years depending on the participant's age. Trained and certified staff administer all assessments following standardized protocols. All participants provided written informed consent, and the study protocol has been approved by the National Institute for Environmental Health Sciences Internal Review Board.

Of 423 participants with brain MRI and wrist-worn accelerometry, 421 (99%; mean age = 71 [*SD* = 18] years) provided valid accelerometer data. Those younger than 65 years of age (n = 106; mean age = 54 [18] years) and those exhibiting cognitive impairment (n = 14; mean age = 82 [8] years) were excluded. The final analytic sample included 301 participants (Supplementary Figure 1).

Accelerometer Variables

Participants were fitted with a wrist-worn Actigraph GT9X monitor (Actigraph, Pensacola, FL) during the last day of their BLSA clinic visit. The monitor, which contains a tri-axial accelerometer sensor, was positioned on the nondominant wrist. Participants were instructed to wear the Actigraph monitor for 7 consecutive days, 24 hours per day. The monitor collects wrist movement in units of gravity (g) at a sampling rate of 80 Hz per second. After the collection period, participants returned the Actigraph monitor to the Clinical Research Unit via express mail. Data were downloaded and preprocessed into 1-minute epoch level activity counts (unitless quantities of movement) using ActiLife Software (version 6.13.4).

Participants with at least 3 valid days were included in this analysis (22). A valid day was defined as having less than 10% missing data. After valid wear periods were determined, each accelerometer minute was label as either "active" if activity counts within that minute reached a threshold of at least 1853 counts per minute or "nonactive/sedentary" if the activity was less than 1853 counts per minute for that minute (23). Activity bouts were defined as contiguous minutes registering as active. Nonactive bouts were defined as contiguous minutes registering as nonactive.

Two summary variables were derived: (a) total active minutes per day and (b) activity fragmentation. Total active minutes per day were calculated by summing the total number of active minutes and calculating the mean across valid wear days for each participant. Activity fragmentation was operationalized as the active-to-sedentary transition probability, calculated as the reciprocal of the average activity bout length for each participant (18,24). "Low," "medium," and "high" categories were derived for both total active minutes and activity fragmentation at their respective tertiles.

Brain Imaging

A 3T Philips Achieva MRI scanner was used for brain imaging. T1-weighted brain scans were acquired using a MPRAGE (magnetization prepared rapid gradient echo) sequence (repetition time [TR] = 6.8 msec, echo time [TE] = 3.2 msec, flip angle = 8°, image matrix = 256 × 256, 170 slices, pixel size = 1 × 1 mm, slice thickness = 1.2 mm).

Anatomical labels and brain volumes (global and regional) were obtained using the Multi-atlas region Segmentation using Ensembles of registration algorithms and parameters (MUSE) approach (25,26). A priori brain regions of interest for this study included total brain, frontal, parietal, temporal, and occipital lobes and the hippocampus in units of a cubic centimeter (cc). Also, gray and white matter volumes were examined within total brain and the lobar regions.

Covariates

Certified and trained study staff collected from participants self-reported age, sex, self-identified race, and years of education. Body mass index (kg/m^2) was calculated using measured weight (kg) and

height (m). Usual gait speed (m/s) was measured over a 6-m course, with the faster of 2 trials used for analysis. Participants self-reported whether they were ever told by a physician or other health professional that they had any of the following conditions: cardiovascular disease including angina, myocardial infarction, congestive heart failure, peripheral arterial disease, and vascular-related procedures; hypertension or high blood pressure; stroke and transient ischemic attack; high cholesterol or triglycerides; chronic bronchitis, emphysema, chronic obstructive pulmonary disease, or asthma; diabetes, glucose intolerance, or high blood sugar; cancer, malignant growth, or malignant tumor; arthritis or osteoarthritis. Responses were summed and categorized into a morbidity index score (0, 1, and 2+ morbid conditions). Depressive symptoms were measured using the 20-item Center for Epidemiologic Studies-Depression scale, ranging from 0 to 60 where a higher score represents higher depressive symptoms (27). Apolipoprotein E (APOE) e4 carrier status was defined as the presence of at least 1 e4 allele versus 0. Baseline intracranial volume (cc), estimated at age 70 years using linear mixed-effects models, was used as a covariate (28). In brief, intracranial volume was the outcome variable with age, time from baseline, and sex treated as predictors. Random effects were included for the intercept and interval.

Statistical Approach

Baseline participant characteristics were descriptively examined by overall sample and low, medium, and high physically active groups. Differences in participant characteristics by groups were tested using analysis of variance for continuous variables and the chi-squared test for categorical variables. Descriptive statistics were calculated for accelerometer characteristics for the entire sample and by low, medium, and high groups of total physical activity (active minutes/day) and activity fragmentation (%).

Multivariable linear regression models were used for all analyses. In all models, each brain volume measure was treated as the independent variable and each physical activity metric as the dependent variable. Separate linear multivariable regression models were constructed to estimate the association between the brain volume variable (cc) and the continuous physical activity metric (eg, active minutes/day or activity fragmentation, %). Covariates were added successively to models. To test whether the association between brain volumes and activity fragmentation was stronger than for total active minutes per day, similar linear regression models were constructed and further adjusted for tertiles of the other physical activity metric (eg, active minutes per day or activity fragmentation). These tertile variables were used to (a) adjust for the degree of fragmentation in the model of active minutes per day and (b) adjust for the volume of daily activity in the model of activity fragmentation, while avoiding collinearity between the continuous variables of time spent active and daily fragmentation ($r = -0.77$). The correlation between the tertile variables of time spent active and daily fragmentation in this sample was $r = -0.61$. Although the tertile analysis accounts for the shared and unique variance that occurs between the 2 physical activity metrics, a sensitivity analysis was also performed to adjust for only the unique variance of each counterpart physical activity variable. Fragmentation adjusted for the time spent active and time spent active adjusted for fragmentation were calculated by using the residuals from 2 separate univariate linear regression models, respectively. For example, to calculate fragmentation adjusted for the time spent active, fragmentation was regressed on time spent active and the resulting residuals were used as an adjusted fragmentation covariate.

Statistical significance was determined using two-tailed hypothesis testing with an alpha level = 0.05. All statistical analyses were performed using STATA software (v. 14.2; Stata Corporation, College Station, TX).

Results

Of the 301 BLSA participants, the mean age was 77 (*SD* = 7) years, 59% were women, and 21% self-identified as Black (Table 1). Participants had a mean of 17 years of education, body mass index of 27 kg/m^2, Center for Epidemiologic Studies-Depression score averaging 4.7, and a usual gait speed of 1.1 m/s. The average number of morbid conditions was approximately 2 with hyperlipidemia, osteoarthritis, and hypertension having the highest prevalence (>62%). Approximately 24% of participants were APOE e4 carriers. Baseline intracranial volume estimated at age 70 years averaged around 1390 cc for the sample. Participants tended to be older and men across tertiles of decreasing physical activity. Those in the lowest tertile of physical activity tended to have a higher prevalence of self-reported cardiovascular disease, diabetes, and osteoarthritis and have larger intracranial volumes.

BLSA participants wore the wrist physical activity monitor for a mean of 6 days for approximately 24 hours per day (Table 2). Participants averaged 7 hours per day in an active state with an activity fragmentation level of 25%. Compared to the low activity tertile, those in the high activity tertile engaged in approximately 3.5 more hours of activity per day. For fragmentation, those in the high fragmentation tertile averaged a 30.8% probability of transitioning from an active to a sedentary state, compared to a 19.4% probability in the low fragmentation tertile.

Total brain, gray matter, and white matter volumes and total, gray, and white matter volumes in the frontal, parietal, and temporal lobes were all associated with total time spent in daily activity (Table 3, Model 1), after adjusting for intracranial volume. After full covariate adjustment (Table 3, Model 3), for every 1 cc higher in total brain volume, 0.35 (*SE* = 0.13; $p = .006$) more minutes per day were spent in daily physical activity. This association with physical activity time was largely detected in the white matter (0.72 [0.23] min/day; $p = .002$), particularly in the parietal (2.60 [1.00] min/day; $p = .008$) and temporal lobes (3.83 [0.94] min/day; $p < .001$).

Total brain, gray matter, and white matter volumes, total, gray, and white matter volumes in the frontal and temporal lobes, and total and white matter volumes in the parietal lobe were all associated with daily activity fragmentation (Table 4, Model 1), after adjusting for intracranial volume. After full covariate adjustment (Table 4, Model 3), for every 1 cc higher in total brain volume, there was an associated 0.02% (*SE* = 0.007; $p = .023$) lower activity fragmentation. This association was observed in total white matter (–0.03% [0.013]; $p = .013$), particularly in the temporal lobe (–0.16% [0.052]; $p = .003$).

Fully adjusted associations presented in Table 3 were attenuated between (a) total brain, (b) total white matter, (c) total and white matter in the parietal lobe, and (d) total and white matter in the temporal lobe with total time spent in daily activity, after additionally adjusting for tertiles of fragmentation in full covariate models (Table 5). Furthermore, the association between gray matter in the parietal lobe and total time spent in daily activity lost significance. In contrast, fully adjusted associations presented in Table 4 between brain volumes and activity fragmentation all lost significance after additionally adjusting for tertiles of active minutes per day in full covariate models (Table 5). However,

Table 1. Overall Participant Characteristics and by Daily Physical Activity

	Overall (n = 301)	High Daily Active Minutes (n = 100)	Medium Daily Active Minutes (n = 100)	Low Daily Active Minutes (n = 101)	p Value for Trend
Age in years, mean (*SD*)	77.2 (7.2)	75.5 (7.2)	77.9 (7.1)	78.1 (6.9)	.01
Women, *n* (%)	177 (58.8)	69 (69.0)	65 (65.0)	43 (42.6)	<.001
Black, *n* (%)	64 (21.3)	27 (27.0)	21 (21.0)	16 (5.8)	.07
Years of education, mean (*SD*)	17.1 (2.5)	16.9 (2.5)	17.3 (2.6)	17.2 (2.4)	.38
Body mass index, kg/m^2, *n* (%)	27.0 (4.6)	27.1 (4.7)	26.3 (4.4)	27.7 (4.7)	.37
No. of morbid conditions, *n* (%)	2.5 (1.3)	2.5 (1.2)	2.3 (1.2)	2.5 (1.5)	.98
0	16 (5.3)	2 (2.0)	8 (8.0)	6 (5.9)	.16
1	52 (17.3)	17 (17.0)	16 (16.0)	19 (18.8)	.87
2 or more	233 (77.4)	81 (81.0)	76 (76.0)	76 (75.3)	.57
Hypertension, *n* (%)	143 (47.5)	56 (56.0)	41 (41.0)	46 (45.5)	.09
Stroke or TIA, *n* (%)	20 (6.6)	5 (5.0)	6 (6.0)	9 (8.9)	.51
Cardiovascular disease, *n* (%)	33 (11.0)	4 (4.0)	13 (13.0)	16 (15.8)	.02
Hyperlipidemia, *n* (%)	187 (62.1)	63 (63.0)	59 (59.0)	65 (64.4)	.72
Pulmonary disease, *n* (%)	32 (10.6)	9 (9.0)	8 (8.0)	15 (14.9)	.23
Diabetes, *n* (%)	49 (16.3)	23 (23.0)	8 (8.0)	18 (17.8)	.01
Cancer, *n* (%)	100 (33.2)	29 (29.0)	32 (32.0)	39 (38.6)	.33
Osteoarthritis, *n* (%)	175 (58.1)	65 (65.0)	61 (61.0)	49 (48.5)	.05
MMSE score ranging from 0 to 30, mean (*SD*)	28.5 (1.3)	28.6 (1.4)	28.5 (1.4)	28.5 (1.3)	.64
CES-D score ranging from 0 to 25, mean (*SD*)	4.7 (4.6)	4.9 (4.5)	4.2 (4.1)	5.0 (5.1)	.76
Usual gait speed, m/s, mean (*SD*)	1.1 (0.2)	1.1 (0.2)	1.1 (0.2)	1.1 (0.2)	.48
Apolipoprotein E e4 risk allele, *n* (%)	71 (23.6)	23 (23.0)	20 (20.0)	28 (27.7)	.43
Intracranial volume, cc, mean (*SD*)	1389.6 (132.1)	1360.1 (129.6)	1375.5 (118.3)	1432.8 (137.6)	<.001

Notes: TIA = transient ischemic attack; MMSE = Mini-Mental State Examination where higher scores represent the higher cognitive mental state (51) (n = 298); CES-D = Center for Epidemiological Studies-Depression where higher scores represent higher depressive-like symptoms (27).

when adjusting for only the unique variance of the counterpart physical activity metric, the statistically significant associations found for both time spent active and fragmentation remain robust (Supplementary Table 1).

Discussion

Our results show that higher brain volumes in the parietal and temporal lobes, largely in white matter, are associated with higher daily physical activity and lower activity fragmentation in well-functioning older adults. The positive associations between brain volumes and the total amount of daily activity remained even after adjusting for activity fragmentation. In contrast, the inverse associations between brain volumes and fragmentation did not remain significant, after adjusting for daily activity minutes. Together, these results suggest that age-related brain atrophy may be reflected in reductions of total daily physical activity accumulation and, to a lesser extent patterns of accumulation, in well-functioning older adults without cognitive impairment.

Studies using objectively measured physical activity show associations with both global and regional brain structures (29–32), primarily observed in the gray matter of the hippocampus (33,34). Along with emerging aerobic physical activity intervention trials (35,36), these findings suggest physical activity can influence brain health. However, it can be postulated that declining cerebral blood flow, brain metabolism, neuroplasticity, and neurogenesis that occurs with structural brain atrophy may partly contribute to age-related declines in everyday physical activity patterns (12). Yet, to the best of our knowledge, only one study led by Arnardottir et al. (30) showed that measurements of either gray or white matter, measured at baseline and over time, were associated with future accelerometer-derived measures of physical activity in older adults. Our findings add to the growing body of literature, by elucidating strong associations between daily activity quantities and patterns and white matter. It is important to note that the low physical activity group had the highest proportion of individuals carrying the APOE e4 allele, a genetic risk factor for Alzheimer's disease and related dementias (37), which might suggest low physical activity may serve as a marker of impending impairment, warranting further longitudinal confirmation. Interestingly, the current study found no associations between gray matter, particularly in the frontal lobe or hippocampus, and physical activity. This difference is likely due to the fairly high usual gait speed—a hallmark indicator of survival (38) and promising marker of lower dementia incidence (39)—observed in this sample of older adults. Additionally, our study examines physical activity broadly as routine movement-based behavior performed throughout the day whereas other studies linking gray matter and frontal lobe regions related to motor function with physical activity focus largely on exercise (ie, physical activity intended for health benefits) and markers of cardiorespiratory fitness (40).

Previously, Spartano et al. (29) found no associations between light-intensity physical activity (the most common type of physical activity in older adults) and hippocampal volume or gray matter in 2354 participants whose mean age was 53 years; almost 25 years younger on average than the BLSA participants in this study. Furthermore, they found that light-intensity physical activity was more strongly related to white matter, specifically to white matter hyperintensities. This

Table 2. Accelerometer Characteristics, *n* = 301

	Mean (*SD*)	Minimum	Maximum
Days of device wear time	5.9 (0.4)	3	11
Device wear time, h/day	23.9 (0.2)	22.7	24
Hours spent physically active (h/day)	7.0 (1.6)	3.4	11.7
Low physical activity (*n* = 101)	5.2 (0.7)	3.4	6.1
Medium physical activity (*n* = 100)	7.0 (0.4)	6.2	7.6
High physical activity (*n* = 100)	8.7 (0.9)	7.7	11.7
Activity fragmentation, %	24.9 (5.3)	12.9	45.7
Low fragmentation (*n* = 101)	19.4 (2.3)	12.9	22.5
Medium fragmentation (*n* = 100)	24.5 (1.1)	22.5	26.7
High fragmentation (*n* = 100)	30.8 (3.7)	26.7	45.7

Notes: Hours spent active and activity fragmentation were tertiled to determine low, medium, and high categories. Activity fragmentation was operationalized as the active-to-sedentary transition probability, calculated as the reciprocal of the average daily activity bout length for each participant (18,24).

Table 3. Association Between Brain Region (cc) and Total Daily Activity (min/day), *n* = 301

	Model 1	Model 2	Model 3
	Beta Coefficient (*SE*) in units of min/day		
Total brain	0.38 (0.11)***	0.33 (0.13)**	0.35 (0.13)**
Gray matter	0.50 (0.17)**	0.30 (0.23)	0.35 (0.22)
White matter	0.73 (0.20)***	0.74 (0.23)**	0.72 (0.23)**
Ventricles	−0.14 (0.27)	0.06 (0.29)	0.11 (0.29)
Frontal	0.73 (0.26)**	0.50 (0.34)	0.49 (0.33)
Gray	1.03 (0.47)*	0.30 (0.59)	0.32 (0.58)
White	1.17 (0.45)*	1.01 (0.53)	0.96 (0.53)
Parietal	1.86 (0.52)***	1.54 (0.61)*	1.81 (0.60)**
Gray	2.55 (0.84)**	1.64 (1.00)	2.31 (0.99)*
White	2.68 (0.92)**	2.48 (1.00)*	2.60 (1.00)**
Temporal	2.14 (0.50)***	2.07 (0.59)**	1.94 (0.59)**
Gray	2.00 (0.81)*	1.19 (0.93)	1.11 (0.93)
White	3.88 (0.86)***	4.02 (0.94)***	3.83 (0.94)***
Occipital	0.96 (0.60)	0.33 (0.68)	0.41 (0.67)
Gray	1.12 (0.92)	−0.26 (1.07)	−0.01 (1.05)
White	2.45 (1.36)	1.93 (1.43)	1.86 (1.42)
Hippocampus	8.27 (7.66)	0.50 (8.68)	2.40 (8.65)
Cerebellum (*n* = 282)	1.04 (0.56)	0.76 (0.60)	0.80 (0.59)

Notes: Model 1 adjusted for intracranial volume (cc). Model 2: Model 1 + age (years), sex, race, education (years). Model 3: Model 2 + body mass index (kg/m^2), depressive symptoms, usual gait speed (m/s), number of morbid conditions, Apolipoprotein E4 status.

*$p < .05$, **$p < .01$, ***$p < .001$.

suggests that myelination degradation may affect connections between gray matter structures (41) that potentially contribute to shrinking daily physical activity routines (29). One possible explanation is that temporal lobe deterioration may lead to impaired memory retrieval (42) and/or auditory and visual processes (43) while parietal lobe degradation may involve compromised spatial awareness, sensory input, and perception (44), all of which may promote decreased confidence and self-efficacy to perform daily activities. Another possible explanation is that the integrity of white matter, its role in functional connectivity for motor function, and related white matter tracts that connect the brain to the musculoskeletal system are compromised (32), an area that has been implicated with gait speed decline in older adults (45–48). Together, these deteriorations may affect the higher-order mental (planning/organizing, intent, and spatial awareness) and physical (coordination, balance, movement) functioning needed to maintain routine physical activity participation.

Temporal white matter and total parietal lobe volumes were also associated with activity fragmentation—a novel pattern of objectively measured physical activity. However, our findings suggest the possibility that these brain regions have more robust associations with total active minutes per day than with daily fragmentation. One explanation is that certain types of sedentary behavior captured by activity fragmentation may be associated with better cognition and brain structure, such as sitting to read a book (49) or resting to recover from higher intensity activity. Another possible explanation is that age-related activity fragmentation may only detect more proximal prodromal symptoms of brain-related diseases and dementias that were not observed in this sample of well-functioning, cognitively intact older adults. Lastly, the association between brain volumes and fragmentation may be stronger earlier in life (eg, later stages of midlife). Collectively, further research is needed to understand the context of fragmentation performed throughout the day, and longer follow-up is needed to evaluate whether fragmentation occurs with early symptoms of mild cognitive impairment and progression to Alzheimer's disease and other dementias in more cognitively impaired populations.

Table 4. Association Between Brain Region (cc) and Daily Activity Fragmentation (%/day), *n* = 301

	Model 1	Model 2	Model 3
	Beta Coefficient (*SE*) in units of %/day		
Total brain	−0.02 (0.006)**	−0.01 (0.007)*	−0.02 (0.007)*
Gray matter	−0.03 (0.010)**	−0.02 (0.013)	−0.02 (0.012)
White matter	−0.03 (0.012)**	−0.03 (0.013)*	−0.03 (0.013)*
Ventricles	0.02 (0.016)	0.01 (0.016)	−0.0002 (0.016)
Frontal	−0.04 (0.015)**	−0.03 (0.019)	−0.03 (0.018)
Gray	−0.07 (0.027)*	−0.04 (0.033)	−0.03 (0.032)
White	−0.05 (0.026)*	−0.05 (0.030)	−0.05 (0.029)
Parietal	−0.08 (0.030)*	−0.06 (0.034)	−0.08 (0.033)*
Gray	−0.12 (0.048)*	−0.06 (0.056)	−0.10 (0.055)
White	−0.09 (0.053)	−0.09 (0.057)	−0.11 (0.055)
Temporal	−0.11 (0.029)***	−0.11 (0.034)**	−0.09 (0.033)**
Gray	−0.13 (0.046)**	−0.10 (0.052)	−0.08 (0.051)
White	−0.15 (0.050)**	−0.17 (0.054)**	−0.16 (0.052)**
Occipital	−0.05 (0.034)	−0.02 (0.038)	−0.02 (0.037)
Gray	−0.07 (0.052)	0.01 (0.060)	−0.008 (0.058)
White	−0.11 (0.078)	−0.09 (0.081)	−0.10 (0.078)
Hippocampus	−0.52 (0.436)	−0.21 (0.490)	−0.28 (0.478)
Cerebellum (*n* = 282)	−0.03 (0.032)	−0.01 (0.034)	−0.01 (0.033)

Notes: Model 1 adjusted for intracranial volume (cc). Model 2: Model 1 + age (years), sex, race, education (years). Model 3: Model 2 + body mass index (kg/m^2), depression, usual gait speed (m/s), number of morbid conditions, and Apolipoprotein E4 status.

*p < .05; **p < .01, ***p < .001.

Table 5. Association Between Brain Region and Each Activity Metric Adjusted for Each Other, Mean (*SD*), *n* = 301

	Physical Activity Amount (min/day)†	Fragmentation (%/day)‡
	Beta Coefficient (*SE*)	
Total brain	0.20 (0.09)*	−0.01 (0.005)
Gray matter	0.12 (0.17)	−0.01 (0.010)
White matter	0.46 (0.18)*	−0.02 (0.010)
Ventricles	0.15 (0.21)	−0.003 (0.01)
Frontal	0.21 (0.25)	0.02 (0.014)
Gray matter	−0.07 (0.43)	−0.04 (0.025)
White matter	0.57 (0.39)	−0.03 (0.023)
Parietal	1.21 (0.45)**	−0.04 (0.026)
Gray matter	1.20 (0.73)	−0.06 (0.042)
White matter	2.02 (0.75)**	−0.06 (0.043)
Temporal	1.11 (0.45)*	−0.03 (0.026)
Gray matter	0.36 (0.70)	−0.04 (0.040)
White matter	2.46 (0.71)**	−0.04 (0.043)
Occipital	−0.20 (0.51)	−0.02 (0.029)
Gray matter	−0.65 (0.79)	−0.03 (0.045)
White matter	0.33 (1.08)	−0.06 (0.062)
Hippocampus	−3.27 (6.53)	−0.36 (0.375)
Cerebellum (*n* = 282)	0.70 (0.44)	0.003 (0.025)

Notes: All models adjusted for intracranial volume (cc), age (years), sex, race (white vs other), education (years), body mass index (kg/m^2), depression, usual gait speed (m/s), number of morbid conditions, and Apolipoprotein E4 status.

†Additionally adjusted for tertiles of fragmentation.

‡Additionally adjusted for tertiles of time spent active.

*p < .05, **p < .01, ***p < .001.

Our cross-sectional findings cannot confirm temporality and warrant a longitudinal investigation into the sensitivity of daily physical activity patterning with brain aging. Other limitations included restricted generalizability of results to well-functioning older adults, unknown activity context of the accelerometer data (eg, sitting vs standing), collection of activity from the wrist may not capture light lower body movements as accurately as ankle or hip monitors, different intensities of physical activity were not assessed and may have different associations with the brain, and accelerometer-based activity thresholds may misclassify activity performed by oldest-old as sedentary. Study strengths include large sample size, use of MRI for brain imaging, and extracting both traditional and novel measures of physical activity patterns from accelerometer data.

In summary, our findings suggest that brain morphometry and physical activity are intrinsically linked, and that sensitive and important structural brain changes potentially indicative of sensorimotor loss may be detected through objective patterns of physical activity deterioration in older adults. More work is needed to examine accelerometry with other aspects of the brain, such as network connectivity (50). Future studies are needed to further elucidate the dynamic, bidirectional relationship between the brain and patterns of physical activity as aging occurs.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

E.M.S., A.P.S., L.F., and J.A.S. currently serve on the editorial board for the *Journal of Gerontology: Medical Sciences*. A.P.S. received an honorarium from Springer Nature Switzerland AG for Guest Editing a Special Issue of *Current Sleep Medicine Reports*. Other authors have no conflicts of interest to disclose.

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