Role of Brain Structure in Predicting Adherence to a Physical Activity Regimen

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ABSTRACT

Objective: Physical activity (PA) is important for maintaining health throughout the lifespan. However, adherence to PA regimens is poor with approximately 50% of older adults terminating activity intervention programs within 6 months. In this study, we tested whether gray matter volume and white matter microstructural integrity before the initiation of a PA intervention predicts PA adherence.

Methods: One hundred fifty-nine adults aged 60 to 80 years were randomly assigned to a moderate-intensity aerobic walking condition or a nonaerobic stretching and toning condition. Participants engaged in supervised exercise 3 times per week for 12 months. Data were collected for a period of 1 year. Voxel-based morphometry and tract-based spatial statistics protocols were used to process neuroimaging data, and ordinary least squares regression models with bootstrapping were used to analyze voxelwise neural predictors of PA adherence.

Results: Greater volume in several regions predicted greater PA adherence, including prefrontal, motor, somatosensory, temporal, and parietal regions ($p < .01$). We also found that higher fractional anisotropy in several white matter tracts predicted greater PA adherence ($p_{\text{FDR-corrected}} < .05$), including the superior longitudinal fasciculus, anterior thalamic radiation, forceps minor, and body of the corpus callosum.

Conclusions: These findings provide preliminary support for macro- and microstructural neural predictors of PA adherence and may translate to other health behaviors and behavioral goal pursuit more broadly.

Key words: adherence, gray matter, physical activity, white matter.

INTRODUCTION

Physical activity (PA) is important for maintaining health and well-being throughout the lifespan (1–3). However, despite the awareness of the long-term health benefits of an active lifestyle, only ~10% of adults meet recommended PA guidelines and ~50% of people starting an exercise regimen stop within 6 months (4,5). Identifying consistent determinants of adherence is essential for designing effective strategies, incentives, and interventions to enhance continued participation in PA.

Research on adherence to PA has focused on contextual and psychological factors, with little emphasis on neurobiological factors. Social-cognitive theory is the most widely used framework for studying psychological motivations for PA adherence, of which self-efficacy is a key construct (6,7). Self-efficacy refers to one's beliefs about his or her capability to successfully perform a specified behavior (8). Indices of exercise self-efficacy have been shown to consistently predict adherence to a PA regimen (7,9).

Importantly, self-efficacy and other social-cognitive factors that influence PA adherence are likely to depend on the integrity of neural networks involved in goal-directed behavior, self-reflection, and self-regulatory capacity, although this has not yet been tested (10–13). Furthermore, biobehavioral models of PA, including the reflective impulsive model and temporal self-regulation theory, emphasize the importance of neurobiological factors for explaining PA adherence (11,14–19). Examining structural neural markers of PA adherence may capture the collective variance in PA adherence explained by self-report instruments of social-cognitive constructs (i.e., self-efficacy, self-regulation). Recent studies, using the novel neuroimaging research methodology known as "brain-as-a-predictor" approach, have shown that measures of neural structure and function can predict long-term health and clinical outcomes, such as smoking cessation, relapse in illicit drug use, and responsiveness to therapy in depressed patients (20). An important assumption underlying this approach is that neural markers serve as objective summary measures of psychological constructs predicting behavioral outcomes. To our knowledge, only one study has applied this brain-as-a-predictor approach to examine whether neuroimaging measures of neural integrity predict PA adherence in the context of structured exercise

ATR = anterior thalamic radiation, **BRAVO** = Bootstrap Regression Analysis of Voxelwise Observations, **DTI** = diffusion tensor imaging, **FA** = fractional anisotropy, **FDR** = false-discovery rate, **MRI** = magnetic resonance imaging, **PA** = physical activity, **PASE** = Physical Activity Scale for the Elderly, **VBM** = voxel-based morphometry

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Received for publication July 22, 2016; revision received August 19, 2017.

DOI: 10.1097/PSY.0000000000000526

programming and found that lateral prefrontal cortex volume predicts better exercise adherence among older women (21).

The aim of the present study was to replicate and extend the findings of Best et al. (21) by applying the brain-as-a-predictor approach to examine whether markers of gray matter and white matter integrity obtained at baseline of a 12-month randomized exercise intervention predicted better intervention adherence in cognitively healthy older men and women. Specifically, we tested whether (1) greater gray matter volume and (2) higher fractional anisotropy (FA), a measure of white matter microstructural integrity, predicted better PA adherence. In a sensitivity analysis, we also tested the extent to which these markers of neural integrity predicted additional variance in PA adherence after accounting for exercise self-efficacy, a consistent predictor of PA adherence. Gray matter consists of neuronal cell bodies, unmyelinated axons, as well as glial cells and capillaries, which support neural function. In contrast, white matter consists of long-range myelinated axons that convey signals between various gray matter regions. We reasoned that gray matter volume and white matter microstructural integrity would be important markers of overall brain health in older adults that may predict PA adherence, given that both gray matter and white matter show age-related degeneration and have both been linked to superior cognitive functioning in older adults (13,14,16,22,23). Specifically, we predicted that greater gray matter volume and white matter microstructural integrity in a broad range of regions relevant to executive function, self-regulation, self-reflection, and PA engagement may be predictive of PA adherence for the 12-month intervention; these may include prefrontal, parietal, and motor regions.

METHODS

Participants

One hundred fifty-nine participants between the ages of 60 and 81 years (mean [SD] age = 66.6[5.6]years) were recruited to participate in a 1-year randomized exercise intervention examining the effects of aerobic fitness training on brain and cognitive health. This study was approved by the University of Illinois Institutional Review Board. Participants were recruited through community advertisements and physician referrals. Potential participants were initially screened over the phone for inclusion and exclusion criteria (see hereinafter for details). Upon passing the initial phone screening, participants were invited to a group orientation to receive study details and ask questions regarding the program. All participants provided informed consent. Three subsequent baseline sessions were performed after the group orientation. The current study focused on the high-resolution structural anatomical magnetic resonance images (MPRAGE) and diffusion tensor imaging (DTI) data collected at baseline before randomization to the intervention and the exercise self-efficacy questionnaires described hereinafter.

Only a subsample (n = 105) of the original sample (N = 159) with MPRAGE, self-efficacy, and adherence data had valid DTI data that could be used to analyze the relationship between white matter integrity and PA adherence. Detailed characteristics of the sample used for DTI data analysis can be found in Oberlin and colleagues (24). The subsample used in the DTI data analysis did not differ from the original sample on demographic characteristics, self-efficacy, or PA adherence.

Investigations of the full sample and subsamples of this trial have also been described in several previous articles (25–29).

Inclusion Criteria

Inclusion criteria for entry into the trial were: 60 years and older, capable of performing physical exercise, physician consent to perform physical exercise, successful completion of a graded maximal exercise test, and be physically inactive at baseline. An inactive life-style was defined as participating in no more than one 20-minute bout of PA per week for the past 6 months.

Exclusion Criteria

Individuals with possible cognitive impairment, as indicated by a score lower 51 on the modified Mini-Mental Status Examination, clinical depression, as indicated by a score 2 or higher on the Geriatric Depression Scale (GDS-5) (30), or impaired vision, as indicated by acuity greater than 20/40 were excluded from the study. In addition, participants who did not meet safety criteria for participating in a magnetic resonance imaging (MRI) study were excluded from the intervention. These criteria include no history of head trauma, head or neck surgery, diabetes, neuropsychiatric or neurological conditions including brain tumors, or having any ferrous metallic implants that could cause injury due to the magnetic field.

Measures

Self-Efficacy

Participant's perceptions of their ability to adhere to an exercise regimen, in the face of barriers, and to engage in PA were assessed using the three self-efficacy scales described hereinafter. These self-efficacy scales are commonly used measures of self-efficacy in the PA literature, and all have good internal consistency ($\alpha \geq 0.93$) (9,17). All self-efficacy scales were administered to participants at the end of the third week of the exercise intervention to ensure accurate assessments of efficacy judgments.

Exercise Self-Efficacy Scale

Exercise self-efficacy scale is an 8-item scale that assesses individuals' belief that they can exercise at moderate intensities 3 times per week for 40+ minutes at 1-week increments over the next 8-week period. This scale is scored on a 100-point percentage scale composed of 10-point increments, ranging from 0% (not at all confident) to 100% (highly confident) (31). A total scale score is derived by summing the responses to each item and dividing by the total number of items in the scale. This measure has been used widely in the social-cognitive literature in understanding PA and has demonstrated outstanding internal consistency (α = .99) (32,33).

Barriers Self-Efficacy Scale

Barriers self-efficacy scale is a 13-item scale used to assess individuals' perceived capabilities to exercise 3 times per week for 40 minutes for the next 2 months in the face of commonly identified barriers to participation. This scale is scored on a 100-point percentage scale composed of 10-point increments, ranging from 0% (not at all confident) to 100% (highly confident). Responses to each item are summed and divided by the total number of items to achieve an overall efficacy strength score ranging from 0 to 100. This scale has good internal consistency ($\alpha \geq .93$) (34).

Life-Style Self-Efficacy Scale

Life-style self-efficacy scale is a 12-item scale used to assess individuals' confidence in their ability to accumulate 30 minutes of PA on 5 or more days of the week for incremental monthly periods. The scale is scored on a 100-point percentage scale composed of 10-point increments, 0 to 100 scale, ranging from 0% (not at all confident) to 100% (highly confident). Responses to each item are summed and divided by the total number of items to achieve an overall efficacy strength score ranging from 0 to 100. The items in this scale have good internal consistency ($\alpha \geq .95$) (35).

Physical Activity Adherence

Adherence reflects the percentage of attendance at exercise classes for the last 11 months of the intervention, given that self-efficacy (a predictor of adherence) was assessed 3 weeks after enrolling in the intervention.

Attendance data were recorded each day by staff, aggregated, and divided by the total possible number of sessions to calculate PA adherence.

Physical Activity Scale for the Elderly

The Physical Activity Scale for the Elderly (PASE) is a 10-item self-report instrument designed to assess PA levels in large samples of older adults (>65 years) for a 1-week period. The PASE combines information from several domains including leisure, household, and occupational functioning. Participants indicate the frequency with which they participated in leisure activities (e.g., outdoor walking; light, moderate, and strenuous sports and recreation; muscle strengthening). The validity of the PASE has been established by studies (36,37) showing an association between PASE scores and several physiological performance indicators, including the following: a sickness impact profile score, grip and leg strength, resting heart rate, age, peak oxygen uptake, percent body fat, and balance.

Self-Efficacy Composite Score

A composite self-efficacy score was created by standardizing and then averaging the self-efficacy scores from each of the three self-efficacy scales: exercise self-efficacy, barriers self-efficacy, and life-style self-efficacy (9,17). The three self-efficacy scales were moderately correlated ($r > .45$ for all scales). See Table 1 for correlations between self-efficacy measures. The composite self-efficacy score was the final variable included in the regression models as a covariate. The composite self-efficacy score was used as a covariate in the regression model to assess the extent to which brain morphology predicts additional variance in PA adherence after accounting for self-efficacy.

Structural MRI

MRI scanning was conducted before the start of the intervention. All participants underwent structural MRI scanning on a 3 T Siemens Allegra scanner. High-resolution (1.3 mm × 1.3 mm × 1.3 mm) T1-weighted brain images were acquired using a three-dimensional magnetization-prepared rapid gradient echo imaging protocol with 144 contiguous slices collected in an ascending fashion.

Diffusion Tensor Imaging

Diffusion-weighted images were acquired using a 3 T Siemens Allegra head-only scanner. The echo time was 94 milliseconds, with repetition time of 4200 milliseconds. Twenty-eight 4-mm slices positioned according to the AC-PC line were obtained along the anterior-posterior commissural plane. The protocol involved a T2-weighted acquisition followed by a 12-direction diffusion-weighted echo planar imaging scan ($b = 1000$ s/mm^2), which was repeated 6 times.

Procedure

Participants came to the laboratory for a 2-hour baseline MRI session within 1 month before the start of the intervention. Structural MR images were collected during this session. During the intervention, participants reported to a university recreation facility 3 times a week for 40-minute sessions to either walk or participate in stretching and toning (control condition). In the walking condition, participants started off by walking for 10 minutes and increased walking duration by 5-minute increments on a weekly basis until a duration of 40 minutes was achieved at week 7. Participants walked for 40 minutes per session for the remainder of the program. All walking was conducted on an indoor track. In the stretching condition, participants engaged in muscle-toning exercises using dumbbells or resistance bands, two exercises designed to improve balance, one yoga sequence, and one exercise of their choice. To keep participants interested, a new group of exercises was introduced every 3 weeks. Three weeks after the start of the intervention, participants were asked to complete exercise self-efficacy questionnaires. Participants then continued to participate in the intervention for 11 more months, at which time total adherence was assessed as the percentage of classes attended during this period.

Analysis

MRI Data Analysis (Gray Matter Volume)

MR data were analyzed to determine the extent to which gray matter volume predicts PA adherence for the 11-month interval. MR data were processed using tools in the FMRIB Software Library (FSL) (Image Analysis Group, FMRIB, Oxford, United Kingdom; http://www.fmrib.ox.ac.uk/fsl/; (38)). An optimized voxel-based morphometry (VBM) protocol was used to analyze structural MRI data (FSL-VBM). An advantage of VBM is that it permits a whole-brain volumetric analysis in a semiautomated manner, making it easy to replicate for researchers with different levels of familiarity with neuroanatomy and does not limit analyses to particular regions of interest. A VBM analysis computes the probability that each voxel in a structural MR image is cerebrospinal fluid, gray matter, or white matter and yields statistical maps for each voxel type (see the study by Ashburner and Friston (39) for a detailed description of VBM methods). Voxels are then classified into the structural category with the highest probability and can be statistically analyzed between individuals.

All images were processed using the following steps: (1) nonbrain matter was removed using the brain extraction technique in FSL (40). (2) All brain-extracted images were visually inspected for any residual nonbrain matter, and any residual matter was then manually removed from the image. (3) Next, these brain-extracted images were segmented into gray matter, white matter, and cerebrospinal fluid using FSL's automated segmentation technique (41). Values were thresholded at greater than.2 to eliminate voxels that are of questionable tissue type. (4) Next, the partial volume estimate maps of gray matter were registered to the Montreal

TABLE 1. Participant Characteristics

	GM-Adherence Sample ($N = 159$)	WM-Adherence Sample ($n = 105$)
	M (SD)	M (SD)
Age, y	66.7 (5.7)	66.6 (5.7)
Years of education	15.8 (2.9)	15.2 (2.9)
Sex (%female)	66%	63%
Exercise self-efficacy	84.1% (18.2%)	76.9% (21.9%)
Barriers self-efficacy	72.7% (19.8%)	68.8% (21.1%)
Life-style self-efficacy	79.0% (21.5%)	73.3% (23.4%)
Attendance	74.9% (17.4%)	74.3% (18.2%)

GM = gray matter; WM = white matter.

Neurological Institute template (42) and followed by nonlinear registration (43) to a study-specific template created from the 159 participants with both MRI and self-efficacy data. (5) Each voxel of each registered gray matter image was modulated by applying the Jacobian determinant from the transformation matrix (44). (6) These modulated images were then concatenated into a four-dimensional image, which was then smoothed using a 3-mm Gaussian kernel. Statistical analyses were then conducted on these segmented, registered, modulated, and smoothed gray matter images. A voxelwise threshold of $p < .01$ and a cluster-based threshold of $p < .05$ were used to determine statistical significance of the associations found in the regression models.

Diffusion Tensor Imaging Data Analysis

Fractional Anisotropy

Diffusion data were processed using FMRIB's Diffusion Toolbox (v.3.0; http://fmrib.ox.ac.uk/fsl/fdt/index.html) in the FMRIB Software Library [FSL v5.0.1], (Image Analysis Group; http://www.fmrib.ox.ac.uk/fsl/; (38)). Voxelwise eigenvalues and eigenvectors of the diffusion tensor from each participant's image were computed, calculating various diffusion parameters, including FA. FA is a commonly used measure of white matter derived from DTI and represents overall anisotropy within a voxel (45). FA values fall between 0 and 1, indicating the degree of microstructural organization, with higher values indicating greater directionality of diffusion.

FA data were fed into the FSL (v4.1.8) tract-based spatial statistics toolbox (v1.2, http://www.fmrib.ox.ac.uk/fsl/tbss/index.html; (46)). Tract-based spatial statistics toolbox is used frequently in DTI processing (46). First, FA images were eroded to remove likely outliers. Then, FA images were normalized to MNI152 standard space. Next, a study-specific template was created and was used as the target for registration. To create the study-specific template, we first registered all native-space FA images to the FA template in Montreal Neurological Institute (MNI) space using an affine warp and then averaged the registered images across individuals to generate the study-specific template. Registration to the study-specific template is conducted by combining two transformations: (1) a nonlinear transformation of each individual's FA image to the study-specific template and (2) an affine registration of the template to MNI152 standard space. After registration, a mean FA image was computed and an average skeleton was generated that represented major tracts common across participants. The skeleton was thresholded at an FA value of 0.2 (46) to ensure that major white matter tracts were included. Then, to account for any residual misalignments not corrected for during registration, each participant's normalized FA image was projected onto the mean FA skeleton. These images were then used in the statistical analyses described hereinafter.

Statistical Analysis

Bootstrap Regression Models

After obtaining the final voxelwise partial volume estimates of gray matter and final FA images projected onto the mean FA skeleton, we tested the association between gray matter volume and PA adherence and white matter microstructural integrity and PA adherence in older adults using the bootstrap regression tool within the Bootstrap Regression Analysis of Voxelwise Observations (BRAVO) toolbox (47,48). Documentation and tutorials for this toolbox are available at https://sites.google.com/site/bravotoolbox. A key benefit of this toolbox is its flexibility to allow for the use of neural data as a predictor, rather than as just an outcome variable. We used identical regression models to test the association of gray matter volume and white matter microstructural integrity with PA adherence. First, we tested whether voxelwise values of gray matter volume (partial volume estimate) and FA would separately predict PA adherence after adjusting for age, sex, education, and self-reported PASE score of PA at baseline using the bootstrap permutation test approach (49,50). For each regression model, 1000 permutation tests were performed per voxel, and in each permutation test, the values in the variable vectors (covariates, gray matter volume, and PA adherence) were independently scrambled. The significance of the association was determined by comparing the distribution of bootstrapped values with the distribution of the original values using a bias-corrected and accelerated method (51).

Clusters of gray matter voxels showing significant associations with PA adherence were identified by using a conservative voxelwise threshold of $p < .01$ and a cluster-based threshold of $p < .05$. This approach uses random field theory and family-wise error to correct for multiple comparisons by determining the probability that the cluster of voxels could occur by chance given the smoothness of the data. To determine significant associations between FA data and PA adherence, we controlled for multiple comparisons ensexed by voxelwise testing using the false-discovery rate (FDR) method. The FDR approach used the p value distributions from our bootstrap regression models and yielded a q value of 0.045. Thus, the significance threshold for all subsequent analyses with FA data was set as $p_{FDR} < .045$.

As a sensitivity analysis, a similar bootstrap permutation approach was used to test the significance of the association between gray matter volume/FA and PA adherence after controlling for self-efficacy. The analysis was conducted to test the extent to which brain-PA adherence relationships were accounted for by self-efficacy, given that it is a key predictor of PA adherence.

RESULTS

Self-Efficacy Predicts PA Adherence

Characteristics of the 159 participants are shown in Table 1. As reported in previous studies using this sample (29), exercise self-efficacy ratings on each of the three self-efficacy scales were independently associated with adherence (all $p < .05$). See Table 2 for correlations between covariates (age and education), self-efficacy scales, and adherence. The association between self-efficacy and adherence did not vary by sex or years of education (all $p > .05$). Age was modestly correlated with adherence ($r = .16$, $p = .04$), such that older participants had higher attendance rates during the intervention. Adherence rates did not significantly differ between men and women ($\chi^2 = 144.88$, $p = .25$). After accounting for variance in adherence associated with age, sex, and education in a linear regression model, a composite score of the three

TABLE 2. Correlations Between Self-Efficacy and PA Adherence in Total Sample ($N = 159$)

	1	2	3	4	5	6
1. Age	—	−0.086	−0.038	−0.095	0.012	0.160*
2. Years of education		—	−0.081	−0.085	−0.069	−0.088
3. Exercise self-efficacy			—	0.454**	0.589**	0.216**
4. Barriers self-efficacy				—	0.455**	0.224**
5. Life-style self-efficacy					—	0.169*
6. Attendance						—

Pearson correlations (2-tailed) *$p < .05$, **$p < .01$.

self-efficacy scales explained 6% of the variance in adherence (adjusted R^2 covariates = 0.017, adjusted R^2 change self-efficacy = 0.056, $\beta = 0.25$, $p = .002$). The association between self-efficacy and adherence did not differ by intervention group when modeling the interaction term (walking versus stretching) (self-efficacy by group interaction $\beta = -0.08$, $p = .54$). Thus, self-efficacy explains adherence to the PA intervention regardless of whether the intervention was moderate-intensity PA or stretching and toning PA. Importantly, adherence rates did not differ by intervention group.

Gray Matter Volume Predicts Adherence to the PA Intervention

We used whole-brain voxelwise regression models with permutation testing in the BRAVO Matlab toolbox to test our hypothesis that gray matter volume in regions supporting self-regulatory, self-efficacy, and other executive processes would predict PA adherence after adjusting for age, education, baseline PA, and sex. Consistent with our hypothesis, greater gray matter volume in a broad range of regions predicted PA adherence, including bilateral precentral and postcentral gyrus, inferior temporal gyrus, temporoparietal junction, and superior parietal lobule (Table 3). After controlling for self-efficacy, volume in many of these regions remained predictive of PA adherence, although a smaller percentage of voxels within each region was associated with PA adherence. After extracting partial volume estimates of regions significantly predictive of PA adherence, we found that gray matter volume explained 18% of variance in PA adherence, even after accounting for self-efficacy ($R^2 = 0.18$). See Figure 1 for a visual comparison of gray matter regions associated with adherence with and without adjusting for self-efficacy. The intervention group assignment did not moderate these associations, so the interaction term modeling group assignment was subsequently dropped from the statistical model.

White Matter Microstructure Predicts Adherence to the PA Intervention

A voxelwise analysis revealed that greater FA in multiple white matter tracts predicted higher attendance rates/better adherence, even after adjusting for age, sex, baseline PA, and years of education. Regions containing clusters predictive of PA adherence included the body of the corpus callosum, the left forceps minor, right external capsule, and bilateral segments of the superior longitudinal fasciculus (SLF), and anterior thalamic radiation (ATR) ($p_{FDR\text{-}corrected} < .05$). Associations between adherence and FA in the superior longitudinal fasciculus, ATR, and body of the corpus callosum persisted after controlling for self-efficacy, although a smaller percentage of voxels within each predicted PA adherence. In contrast, the association between the left forceps minor and PA adherence was no longer significant after including self-efficacy in the model. Figure 2 shows the spatial distribution of statistically significant clusters within the white matter skeleton that predicted PA adherence both before and after adjusting for self-efficacy (Table 4).

DISCUSSION

We tested the hypothesis that greater gray matter volume and white matter microstructural integrity would predict better adherence to a 12-month exercise intervention in older adults. Consistent with this prediction, greater gray matter volume in frontal, temporal, and parietal regions was predictive of better adherence to the intervention, irrespective of intervention group. Gray matter volume in many of these regions remained predictive of adherence after accounting for self-efficacy, although the percentage of voxels predictive of adherence declined. Higher white matter microstructural integrity in a wide array of tracts was also predictive of PA adherence, including the body of the corpus callosum, ATR, superior longitudinal fasiculus, and forceps minor. Most of these associations remained significant after controlling for self-efficacy.

The aim of this study was to explore whether there is a neurobiological basis for continued participation in PA. Although only one previous study has examined neural predictors of PA (21), recent efforts (11,52) have explored cognitive predictors of PA and have shown that cognitive control and self-regulatory processes that are critical for initiating and maintaining PA are supported by widely distributed brain networks spanning across the frontal, temporal, and parietal lobe (i.e., frontal-parietal network, cingulo-opercular

TABLE 3. Gray Matter Clusters Predicting PA Adherence

Gray Matter Region	Laterality	Cluster Size (Voxels)	Peak *Z*	MNI Coordinates (COG)		
				X	*Y*	*Z*
Gray matter volume						
Predicting PA adherence						
Precentral/postcentral gyrus	Left	4563	5.03	−40	−30	52
Inferior temporal gyrus	Right	3050	5.16	18	−42	−30
Inferior temporal gyrus	Left	1328	3.66	−38	−2	−34
Precentral/postcentral gyrus	Right	1068	3.98	50	−18	44
Gray matter volume						
Predicting PA adherence independent of SE						
Inferior temporal gyrus	Right	1383	4.7	30	−34	−30
Middle frontal/precental/postcentral gyrus	Left	1325	3.64	−32	−16	62
Inferior temporal gyrus	Left	1149	3.62	−36	0	−36

PA = physical activity; COG = center of gravity.

VBM used to estimate gray matter clusters predictive of PA adherence using a voxelwise threshold $p < .01$, cluster threshold $p < .05$.

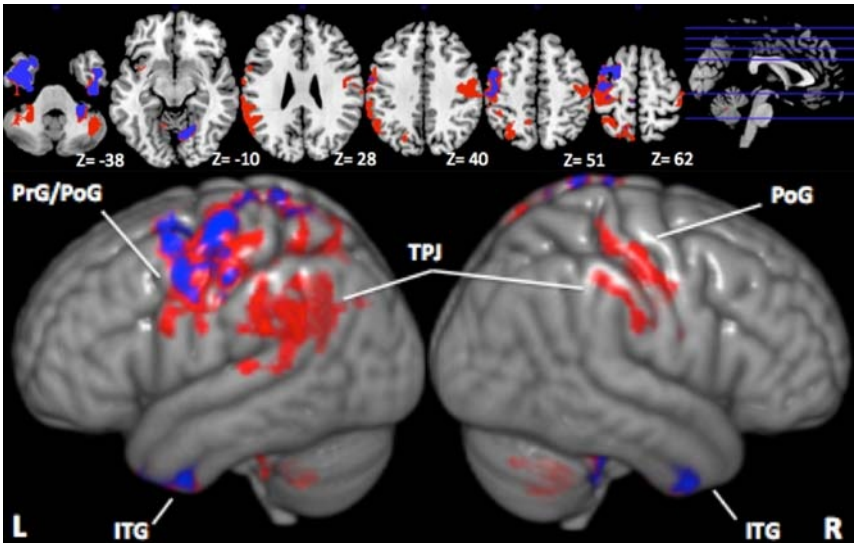

FIGURE 1. Gray matter regions predictive of PA adherence (top row: axial slices, bottom row: 3D sagittal view). PrG = precentral gyrus, PoG = postcentral gyrus, TPJ = temporoparietal junction, ITG = inferior temporal gyrus. Red represents GM regions predicting PA adherence that no longer remained significant (voxelwise threshold $p < .01$, cluster threshold $p < .05$) after controlling for SE. **Blue** represents GM regions that remained statistically significant (voxelwise threshold $p < .01$, cluster threshold $p < .05$) predictors of PA adherence after controlling for SE. Regions predicting PA adherence were left lateralized (Table 3). Color image is available only in online version (www.psychosomaticmedicine.org).

network, and default-mode network) (see the study by Hare et al. (11) for review). The present findings contribute to this literature by showing that regions that predict PA adherence significantly overlap with several networks associated with cognitive control and self-regulatory processes.

The gray matter regions we found to predict PA adherence, including the regions around the intraparietal sulcus, the precentral gyrus, and lateral prefrontal cortex have been functionally linked as part of a "multiple-demand" system by Duncan and colleagues (53–55) through resting state and task-evoked functional MRI studies. These studies show that these regions may collectively represent a domain general network linked to cognitive control processes that are involved in a variety of behaviors, such as selective attention, maintenance of goals, and performance monitoring. The overlap between our gray matter findings and previous work identifying the multiple-demand system suggests that preservation of gray matter in these regions may not only be particularly beneficial for PA adherence but may be more broadly implicated in a number of processes involved in behavioral goal pursuit. The attenuation of some of these gray matter associations with adherence after accounting for self-efficacy is striking, given that self-efficacy only explained a modest amount of variance in PA adherence; this pattern may suggest that the self-efficacy–PA adherence relationship may partially mediate the relationship between gray

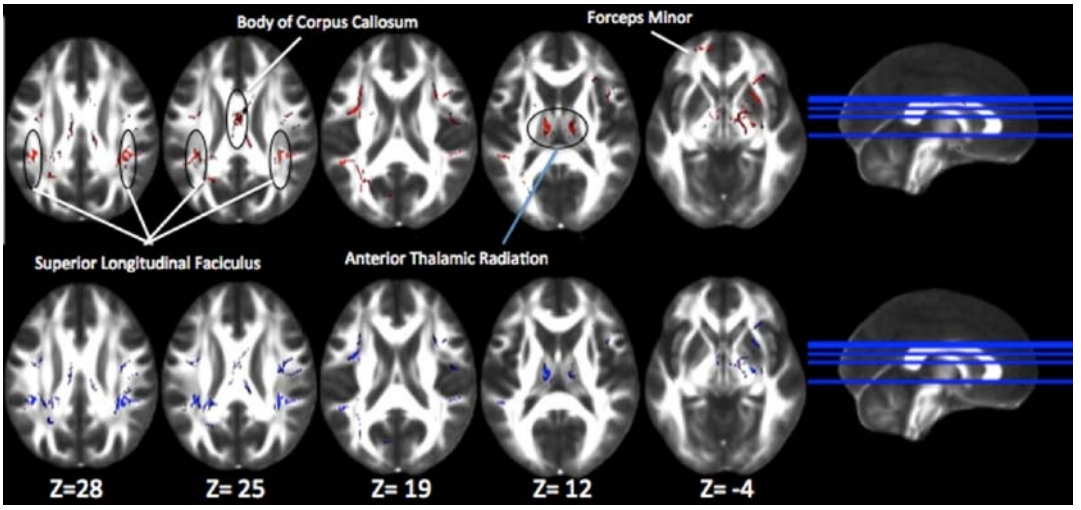

FIGURE 2. White mater microstructural integrity predicts PA adherence. RED represents regions in which integrity of white matter microstructure was predictive of PA adherence before controlling for self-efficacy ($p_{FDR\text{-}corrected} < .05$). Blue represents regions in which integrity of white matter microstructure was predictive of PA adherence after controlling for self-efficacy ($p_{FDR\text{-}corrected} < .05$). Color image is available only in online version (www.psychosomaticmedicine.org).

TABLE 4. White Matter Regions Predicting PA Adherence

White Matter Tract	Laterality	Cluster Size (Voxels)	Max *p*	MNI Coordinates (COG)		
				X	*Y*	*Z*
Predicting PA adherence						
Posterior corona radiata	Left	1564	0.999	−40	−30	52
Anterior thalamic radiation	Right	1024	0.996	18	−42	−30
Anterior thalamic radiation	Left	608	0.999	−33	−50	24
Body of corpus callosum	Right	553	0.99	14	−10	3
Superior longitudinal fasiculus	Left	550	0.998	−8	−14	8
Superior longitudinal fasiculus	Left	484	0.999	−4	−9	27
Inferior fronto-occipital fasiculus	Left	479	0.999	−34	2	20
Superior longitudinal fasiculus	Right	466	0.998	39	−40	26
Superior longitudinal fasiculus	Right	315	0.99	32	27	1
Inferior fronto-occipital fasiculus/uncinate fasiculus	Right	302	0.998	39	12	15
Forceps minor	Right	268	0.998	44	−9	23
Predicting PA adherence independent of SE						
Superior longitudinal fasiculus	Left	894	0.999	−35	−40	24
Anterior thalamic radiation	Left	571	0.999	−8	−14	8
Superior longitudinal fasiculus	Right	487	0.999	39	−39	25
Superior longitudinal fasiculus	Right	480	0.994	43	−10	23
Superior longitudinal fasiculus	Left	453	0.998	−35	−2	22
Superior longitudinal fasiculus	Right	337	0.993	39	12	15
Anterior thalamic radiation/corticospinal tract	Right	282	0.995	20	−9	−4

COG = center of gravity.

FSL Tract-Based Spatial Statistics and BRAVO toolbox used to identify clusters of white matter regions in which FA values were predictive of adherence (p_{FDR} = .05). Table is limited to clusters including > 200 voxels.

matter volume and adherence, although this needs to be tested in future studies.

We also found that integrity of white matter microstructure in widely distributed white matter tracts was predictive of PA adherence. These regions included the temporal portion of the superior longitudinal fasiculus, which partially overlapped with gray matter regions we found to be predictive of PA adherence in the superior temporal cortex (see *Z* = 28 in Figures 1, 2), suggesting that structural integrity of both gray matter and white matter in this region predicts PA adherence. Other white matter tracts that we found to predict PA adherence include the body of the corpus callosum, which facilitates interhemispheric communication, the ATR, which is involved in reciprocal communication of limbic regions with prefrontal and anterior cingulate cortex, and the forceps minor, which is involved in communication between lateral and medial prefrontal regions. Interestingly, white matter integrity in the forceps minor became nonsignificant after covarying for self-efficacy, suggesting that the self-efficacy–PA adherence relationship may be supported by structural connectivity between lateral and medial prefrontal regions, although this needs to be further explored. Importantly, integrity of all of these tracts is critical for the preservation of cognitive control processes in late life (56–58). In turn, these cognitive control processes are involved in self-regulation of a variety of goal-directed behaviors. Similar to the gray matter findings, the breadth of white matter tracts in which microstructural integrity was predictive of PA suggests that these findings may extend beyond PA to goal pursuit more generally.

These findings also support the brain-as-a-predictor approach to understanding real-world behavioral phenomenon (20). The aim of this methodological approach is to leverage objective measures of neural structure and function to predict long-term, ecologically valid outcomes that extend beyond laboratory testing. The advent of neuroimaging technology affords the possibility to link objective neurobiological markers to behavior in a variety of domains, including cognitive function, health (i.e., smoking cessation), economic decision making, and clinical and neurological outcomes (20). Our findings contribute to this literature by showing that macro- and microstructural integrity of neural architecture in widely distributed networks predict PA adherence, many of which support cognitive control and self-regulatory processes.

The findings from the present study have shown that older adults with greater gray matter volume and white matter microstructure in regions supporting cognitive control and self-regulation show better adherence to a yearlong structured PA intervention. These associations were also found to be statistically independent of randomization, such that gray matter volume and white matter integrity were predictive of better adherence regardless of whether participants were in the walking group or the stretching and toning group. The implications of these associations may also extend beyond PA adherence, to include the adoption and maintenance of other healthy life-style behaviors that are protective against physical and cognitive health decline. In turn, macro- and microstructural integrity in these regions may broadly influence quality of life and participation in health behaviors more generally.

Future research can extend these findings by examining the extent to which gray matter and white matter regions predictive of adherence show PA-induced volumetric changes and whether such brain changes positively influence cognition. This will help us understand whether the relationship between brain health and adherence affects exercise-induced improvements in brain health. One possibility is that older adults with greater gray matter atrophy and white matter degeneration in regions supporting self-efficacy and self-regulatory strategies may not show as much exercise-related improvements in gray matter and white matter because of poor adherence. To address this, interventions could be tailored to focus on improving self-efficacy during the initial phases of the intervention and by improving self-regulatory skills, such as planning and goal setting. On the other hand, individuals with greater gray matter atrophy and white matter degeneration in these regions may show similar levels of improvement in brain health as those with less atrophy. This could indicate that those with poorer brain health have "more to gain" from the exercise intervention, relative to those with better brain health. Future research can also expand on this study by examining the relationship between structural neural markers of adherence and other psychological predictors of PA adherence (i.e., self-regulatory strategies, executive functions). Examining which cognitive variables that are most related to neural markers of PA adherence may highlight efficient and cost-effective behavioral measures that investigators could use to identify those participants most likely to adhere, or not adhere, to a long-term structured PA intervention.

Limitations and Summary

There are several limitations to the present study. First, the brain regions identified here are related to executive function, self-regulation, emotional control, reward, and other psychosocial, affective, and cognitive processes, and we cannot determine the psychological constructs that are linked both to these regions and to adherence. Moreover, we did not account for cardiometabolic risk factors that are associated with both reduced gray and white matter integrity and sustained physical inactivity in this study. We see the outcomes from this study as an important first step in characterizing the neural correlates of PA adherence, but more research is needed before definitive conclusions can be made. Next, this was a 12-month intervention, and it is unclear whether these same associations would occur for trials of a different type, duration, or intensity (e.g., resistance training). This study was also conducted using a mostly white sample of highly educated healthy older adults from a midwestern city; therefore, these results may not be easily generalizable to more culturally diverse, younger, and clinical populations. There are a number of additional limitations related to the MRI analysis methods used in this study. First, VBM only provides estimates of tissue type and does not provide absolute values of volume. In addition, the diffusion data were collected using only 12 gradient directions, which limits the precision of the tensor estimation. Furthermore, a FLAIR sequence was not run, so we could not control for white matter hyperintensities.

In summary, we found that gray matter volume and white matter microstructural integrity in a broad range of frontal, temporal, and parietal regions predicted adherence to a yearlong structured PA intervention in older adults. Many of these regions support executive control, self-regulatory processes, and voluntary motor function. These findings provide preliminary support for neural substrates underlying PA adherence in the context of structured exercise programming. Future research will need to expand on these findings by examining how these associations affect exercise-related improvements in brain health.

Source of Funding and Conflicts of Interest: This work was supported by the National Institute on Aging at the National Institutes of Health (RO1 AG25667, RO1 AG25032) awarded to A.K. and E.M. S.G. was supported by the National Science Foundation Graduate Research Fellowship Program under Grant Number 2014192810. K.I.E. was supported by research grants (R01 DK095172, P30 AG024827, P30 MH90333). The authors report no conflicts of interest.

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