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Research report

Association of change in brain structure to objectively measured physical activity and sedentary behavior in older adults: Age, Gene/Environment Susceptibility-Reykjavik Study

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HIGHLIGHTS

- Accelerometer was used to measure physical activity and sedentary behavior at follow up.
- Gray matter and white matter was measured both at baseline and follow up, with 5-year interval.
- An association was found between brain atrophy and physical activity.
- There was also an association between brain atrophy and sedentary behavior, independent of lifestyle physical activity.

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ABSTRACT

Many studies have examined the hypothesis that greater participation in physical activity (PA) is associated with less brain atrophy. Here we examine, in a sub-sample ($n = 352$, mean age 79.1 years) of the Age, Gene/Environment Susceptibility-Reykjavik Study cohort, the association of the baseline and 5-year change in magnetic resonance imaging (MRI)-derived volumes of gray matter (GM) and white matter (WM) to active and sedentary behavior (SB) measured at the end of the 5-year period by a hip-worn accelerometer for seven consecutive days. More GM ($\beta = 0.11$; $p = 0.044$) and WM ($\beta = 0.11$; $p = 0.030$) at baseline was associated with more total physical activity (TPA). Also, when adjusting for baseline values, the 5-year change in GM ($\beta = 0.14$; $p = 0.0037$) and WM ($\beta = 0.11$; $p = 0.030$) was associated with TPA. The 5-year change in WM was associated with SB ($\beta = -0.11$; $p = 0.0007$). These data suggest that objectively measured PA and SB late in life are associated with current and prior cross-sectional measures of brain atrophy, and that change over time is associated with PA and SB in expected directions.

Abbreviation: AGES-Reykjavik study, Age, Gene/Environment Susceptibility Reykjavik Study; AGESII-Reykjavik study, Age, Gene/Environment Susceptibility Reykjavik Study, second phase; BMI, body max index; CSF, cerebral spinal fluid; DP, diastolic pressure; GM, gray matter; ICV, intra-cranial volume; MAP, mean arterial pressure; MRI, magnetic resonance imaging; SB, sedentary behavior; SP, systolic pressure; SPA, self-reported PA questionnaire; PA, physical activity; WM, white matter; WMH, white matter hyperintensities.

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1. Introduction

It is hypothesized that physical activity (PA) helps to preserve and maintain cognitive function and decrease the risk of dementia and Alzheimer disease [1–4]. Change in cognitive ability has been associated with brain atrophy [5–17]. It has been shown that the brain atrophies with age due to volume loss in both white (WM) and gray matter (GM) and increase in white matter lesions [18]. GM has been shown to linearly decline with increasing age starting at early adulthood, while WM deterioration shows nonlinear changes [14,19,20]. WM has been shown to increase throughout adulthood, peaking at around the age of 40–60 years, followed by an accelerated decline starting around age 60 [14,19]. PA is also known to be negatively associated with age [21,22] and sedentary behavior (SB) is known to be positively associated with age [23]. This trend has been shown to start in the forties [22].

Cross-sectional studies have shown a positive relationship between GM and WM volumes in the older adult brain and physical fitness [24,25]. Furthermore, six months aerobic training was shown to increase both GM and WM volumes in older subjects [26]. A cross-sectional study, using questionnaire, showed PA levels to positively correlate with brain volumes [27]. Longitudinal studies, using questionnaires have shown that higher level of PA at baseline predicts larger GM volume [28–30], larger WM volume [29] and more total brain volume [29,30] in late life. Studies using objectively measured PA are needed to confirm these results.

Previous studies have shown that lower PA levels predict lower brain volumes and atrophy [28–30], indicating that PA affects brain volumes. Currently, there are no published studies on whether brain volumes or changes in brain volume, is associated with PA later in life. It might be expected that those with greater PA would have a history of greater brain volumes both in the past and in the present and show the best maintenance of brain volumes over time. The aims of this study are to quantify the prospective changes in magnetic resonance imaging (MRI)-derived brain atrophy measurements in a 5-year period and explore their association with objectively measured PA and SB in an older population. This study is the first to assess brain atrophy in a longitudinal study design in relation to objectively measured behavior outcomes. Furthermore, we will test the hypothesis that the association between brain volumes and the important behavioral variables, PA and SB, are independent of self-reported PA at baseline (SPA).

2. Methods

2.1. Study population and design

The Age, Gene/Environment Susceptibility Reykjavik Study (AGES-Reykjavik study) was a prospective cohort study designed to examine risk factors in relation to disease and disability in old age. The aim was to investigate the contributions of environmental factors, genetic susceptibility, and gene-environment interactions to aging of the neurocognitive, cardiovascular, musculoskeletal, body composition, and metabolic systems. The AGES-Reykjavik study is a continuation of the Reykjavik Study, which was initiated in 1967 by the Icelandic Heart Association and included men and women born in 1907–1935 and living in the Reykjavik area. From 2002 to 2006, new data were collected for the AGES-Reykjavik study, and details on the study design have been described elsewhere [31]. Data from this data collection was used as baseline measurements for the current study. The current study was a part of the AGESII-Reykjavik study which is a follow up of the AGES-Reykjavik study, with the time interval of approximately five years. Between April 2009 and June 2010, objective PA measurement by accelerometers was added to the AGESII-Reykjavik study test protocol [21]. During the PA sub-study measurement period, 1194 subjects participated in the AGESII-Reykjavik study and were eligible to be invited to participate in the sub-study. Of these, 150 participants were excluded for different reasons (e.g., blindness and other physical- and mental impairments), 84 refused and 294 did not participate because of scheduling conflicts. Five subjects lost the accelerometers. The remaining 671 (56.2%) participants received an accelerometer to measure their daily activity. Of these, 585 participants had four or more valid days ($\geq$10 h of wear time) of useable accelerometry data. After excluding those with mild cognitive impairment (MCI), dementia or scored 24 or less on MMSE, 18 or less on the DSST test and did not have both brain measurements in AGES-Reykjavik study and AGESII-Reykjavik study, the final number of subjects was 352. The study was approved by the Icelandic National Bioethics Committee (VSN: 00-063), the Icelandic Data Protection Authority, and the institutional review board of the US National Institute on Aging, National Institutes of Health. Signed informed consent was given by all participants.

2.2. Assessment of PA

Participants were asked to wear the ActiGraph GT3X accelerometer (Actigraph Inc., Pensacola FL) monitor at the right hip for one complete week and to remove the monitor only before going to bed and during showers, bathing, or other water activities. Non-wear was defined as a period of at least 60 consecutive minutes during which the activity monitor recorded zero counts in all axes, allowing 1–2 min of vertical-axis counts between 0 and 100. A day of accelerometer wear was considered valid if the wear time was $\geq$10 h. Participants with fewer than four valid days over the week of measurement were excluded. Activity variables were derived from vertical-axis count values, and included: Total PA (TPA) defined as total counts during an average day (counts $\times$ day^{-1}) and SB as hours $\times$ day^{-1} of activity <100 count $\times$ min^{-1} during wear time. Lifestyle PA was defined as $\geq$760 counts $\times$ min^{-1} [21,32,33].

2.3. MRI image acquisition

MRI including T1-, proton density-, and T2-weighted and fluid-attenuated inversion recovery (FLAIR) images were acquired on a 1.5-Tesla Signa Twinspeed EXCITE system (General Electric Medical Systems, Waukesha, WI) in the AGES-Reykjavik study. Brain tissue volumes, including GM, WM, cerebral spinal fluid (CSF), and white matter hyperintensities (WMH), were generated separately, using the multispectral MR images and a high-throughput automatic image analysis pipeline, which is based on the Montreal Neurological Institute (MNI) pipeline and optimized for use in the AGES-Reykjavik study (AGES-RS/MNI pipeline) [18]. The key processing stages were as follows: stereotaxic registration was achieved after signal non-uniformity correction by an affine transformation of the T1-weighted images to the ICBM152 template. Intersequence registration was performed by registering images from the individual (T2/proton density, fluid-attenuated inversion recovery) sequences to the T1-weighted images in order to accurately align all image volumes acquired during an acquisition session. Linear signal intensity normalization was then applied to correct for signal intensity variations across images in the different sequences. Finally, tissue classification was achieved with an artificial neural network classifier. The absolute volumes of the four tissue types were subsequently calculated and converted to native space volumes using the scale factor obtained from the stereotaxic registration transformation. Intra-cranial volume (ICV) was calculated by adding the volumes of GM, normal WM, WMH and CSF. All tissue volumes are presented as percent of the total ICV. The acquisition and post-processing of the MRI have been described in detail