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Research report

Objective measures of physical activity, white matter integrity and cognitive status in adults over age 80

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HIGHLIGHTS

- We examined physical activity components in relation to white matter integrity.
- More steps and longer duration were associated with greater white matter integrity.
- Associations were localized in frontal and temporal areas.
- Associations were independent of cardiometabolic conditions and physical limitation.

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ABSTRACT

The neuroprotective effects of physical activity (PA) are consistently shown in older adults, but the neural substrates, particularly in white matter (WM), are understudied, especially in very old adults with the fastest growth rate and the highest risk of dementia. This study quantified the association between PA and WM integrity in adults over 80. The moderating effects of cardiometabolic conditions, physical functional limitations and WM hyperintensities were also examined, as they can affect PA and brain integrity. Fractional anisotropy (FA) from normal-appearing WM via diffusion tensor imaging and WM hyperintensities were obtained in 90 participants (mean age = 87.4, 51.1% female, 55.6% white) with concurrent objective measures of steps, active energy expenditure (AEE in kcal), duration (min), and intensity (metabolic equivalents, METs) via SenseWear Armband. Clinical adjudication of cognitive status, prevalence of stroke and diabetes, systolic blood pressure, and gait speed were assessed at time of neuroimaging. Participants were on average sedentary (mean ± SD/day: 1766 ± 1345 steps, 202 ± 311 kcal, 211 ± 39 min, 1.8 ± 1.1 METs). Higher steps, AEE and duration, but not intensity, were significantly associated with higher FA. Associations were localized in frontal and temporal areas. Moderating effects of cardiometabolic conditions, physical functional limitations, and WM hyperintensities were not significant. Neither FA nor PA was related to cognitive status. Older adults with a sedentary lifestyle and a wide range of cardiometabolic conditions and physical functional limitations, displayed higher WM integrity in relation to higher PA. Studies of very old adults to quantify the role of PA in reducing dementia burden via WM integrity are warranted.

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1. Introduction

Loss of white matter (WM) integrity in frontal and medial temporal brain areas is related to difficulties in working memory and impaired processing speed [1,2]. Although working memory and processing speed decline more rapidly with older age, these cognitive domains have also been shown to improve in response to greater amounts of physical activity (PA) (for review, see [3]). However, associations between PA and white matter (WM) integrity and cognitive function have not been studied among octogenarians. With soaring incidence rates of dementia among adults aged 80 and older [4] and the sheer increase in the growth rate of this segment of the population [5], it is essential to rapidly identify strategies to promote cognition and WM integrity for these adults. Characterizing the relationship between objective measures of PA and WM integrity and cognition for these adults can also improve the design of targeted PA guidelines and prescriptions. With more than half adults aged 85 and over being able to walk [6], PA interventions appear feasible [7,8]. However, PA trials targeting very old adults to improve cognition appear premature at this time; most evidence to date is for younger and healthier old adults, with little information on the relative impact of other common health-related conditions on these associations.

Positive associations of higher PA with greater WM volume and fewer WM lesions have been reported in adults in their 60s and 70s [9–12]. A small intervention study shows exercise training increases WM volume [13]. Higher PA has also been associated with greater WM integrity using diffusion tensor imaging (DTI) in two descriptive studies [10,14] and in one fitness intervention trial aiming to increase walking [15] in adults younger than 80. Although very promising, these studies provide limited information on the potential PA beneficial effects for adults 80 and older, not only because of the few adults 80 and older examined, but also because the roles of cardiometabolic conditions, dementia, or physical functional limitations was not examined. This is critically important because chronic disease conditions and physical function limitations compromise the ability of older adults to safely engage in PA and may also affect WM integrity.

Another limitation of prior studies is the use of relatively crude measures of WM and of PA. The use of self-report PA measures cannot distinguish duration from intensity and cannot accurately assess low intensity or short duration of PA, commonly seen in this age group. Furthermore, self-report measures require recall accuracy which is challenging for older persons with declining memory functions. One recent study using accelerometry reported that light PA was associated with greater temporal WM integrity in adults in their mid-sixties [16]. Although objective, accelerometer only provides a crude measure of the activity counts. Similarly, by focusing on WM macrostructure, prior studies have mostly provided information on overall WM volume or radiologically overt lesions. Compared to crude measures of WM lesions and hyperintensities, DTI provides more accurate measures of brain parenchyma microstructure and it has been related to earlier stages of cognitive impairment [17]. Disruption of WM integrity is frequently observed as decreased fractional anisotropy (FA), commonly resulted from increased radial diffusivity (RD) or decreased axial diffusivity (AD). Increased RD may indicate demyelination, whereas decreased AD suggests axonal damage [18]. Therefore, the application of DTI can help uncover the mechanisms underlying the relationship between PA and WM integrity.

The objective of this study was to examine the cross-sectional association between objective multidimensional measures of PA and WM integrity measured as FA using DTI, and cognitive function, in a cohort of adults over 80 years old with extensive retrospective clinical and cognitive data over the prior 14 years. It was hypothesized that higher active energy expenditure (AEE), more step counts, longer duration and higher intensity of PA would be associated with lower dementia prevalence and higher FA. We further hypothesized these associations would be stronger for frontal and medial temporal areas than other areas. A second objective was to examine the roles of cardiometabolic conditions, dementia, and physical functional limitations as potential modifiers of these associations.

2. Methods

2.1. Study population

Participants were recruited from the Health, Aging and Body Composition Study cohort, an ongoing longitudinal study that began in March 1997 to assess the relationship between changes in body composition and health outcomes in 3075 community-dwelling older adults (52% female, 42% black) aged 70–79 years [19]. Among 1527 participants entering the study at the Pittsburgh site, 819 were alive and seen in the clinic or had a home visit in 2006–2008. Of the 819, 315 received a brain Magnetic Resonance Imaging (MRI) scan at 3 Tesla [20] and 10 received a brain MRI at 1.5 Tesla because joint replacements or implants had not been cleared for safety at 3 Tesla as part of the Healthy Brain Project. Of the 819, 99 did not meet the eligibility for a brain MRI. 169 were ineligible for the Healthy Brain Project because they were walking with a cane and/or did not have mobility performance measures (this served as exclusion criteria as the original study was designed to investigate mobility). 145 were not interested in participating in the brain MRI or refused. 17 were not scanned either because of intervening illness, death before the scan, or because they changed their mind, although eligible. 64 were not included either because of hospitalization for major clinic events in the previous three months (fracture, psychiatric problem) or for other reasons (missing data).

In 2010–2012, 163 participants received a follow-up MRI with DTI and were offered the SWA assessment. Of the 163, 103 were eligible and interested in wearing a SenseWear Armband (SWA). 90 out of 103 had usable SWA data with at least 3-day on-body time [21] as well as DTI data and were included in this study (Supplementary Figure 1). All participants provided written informed consent. The University of Pittsburgh Institutional Review Board approved the protocol. The average interval between SWA and the follow-up MRI was 7.7 months (SD = 6.3). Age was obtained at time of the SWA measurement. Sex, race, and education were obtained at the Health, Aging and Body Composition Study entry examination.

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.bbr.2015.01.045.

2.2. MRI acquisition

MRI scans were obtained at the MR Research Center of the University of Pittsburgh with a 3 Tesla Siemens TIM TRIO scanner equipped for echo-planer imaging using the protocol previously described [20]. DTI were acquired using single-short spin-echo echo planar imaging sequence with the following parameters: TR = 5300 ms; TE = 88 ms; TI = 2500 ms; Flip angle = 90°; FOV = 256 mm × 256 mm; two diffusion values of $b = 0$ and 1000 s/mm^2; 12 diffusion directions; four repeats; 40 slices; matrix size = 128 × 128; voxel size = 2 mm × 2 mm; slice thickness = 3 mm; and GRAPPA = 2. Two series of sagittal scans (with and without the off-resonance saturation pulse with an offset frequency of 1.5 kHz) were obtained for the MT acquisition across 120 slices with matrix size = 256 × 192; TR = 35 ms; TE = 2.86 ms; TI = 300 ms; Flip angle = 15°; slice thickness: 1.5 mm; voxel size = 0.89 mm × 0.89 mm; and FOV = 230 mm × 230 mm.