Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring 4 (2016) 14-17

Alzheimer's & Dementia

Diagnostic Assessment & Prognosis

Meeting physical activity recommendations may be protective against temporal lobe atrophy in older adults at risk for Alzheimer's disease

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Abstract

Introduction: Physical activity (PA) is associated with brain health in older adults. However, it is unknown whether the current physical activity recommendations (PAR) impart substantive benefit. The objective of this study was to compare temporal lobe volumes between older adults who met PAR and those who did not.

Methods: Ninety-one enrollees from the Wisconsin Registry for Alzheimer's Prevention wore an accelerometer for seven consecutive days to quantify their PA behaviors and underwent a T-1 anatomic magnetic resonance imaging scan. Participants were categorized as either having met PAR or not based on the US Department of Health and Human Services recommendations of 150 minutes of moderate-to-vigorous physical activity per week.

Results: Participants who met PAR possessed significantly greater inferior ($\eta^2_P = .050$) and anterior ($\eta^2_P = .055$) temporal lobe volumes compared with those who did not ($P < .05$).

Discussion: Individuals at-risk for AD experience accelerated rates of brain atrophy. These results suggest that regular engagement in PA at or above PAR could attenuate this decline.

Keywords: Dementia; Alzheimer's disease; Exercise; Family history; *APOE* ε4; Neuroimaging

1. Introduction

Alzheimer's disease (AD) affects more than 5 million Americans and that number is projected to nearly triple by 2050 [1]. A hallmark feature of AD is brain atrophy, which typically precedes the onset of symptoms [2,3] and is a predictor of future cognitive impairment [4,5]. Physical activity (PA) and fitness may mitigate brain atrophy as both have been positively associated with gray matter volume in older adults [6,7] and older adults at-risk for AD [8]. However, the influence of meeting physical activity recommendations (PAR) via accelerometry on brain volume

The authors have no conflicts of interest to disclose.

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http://dx.doi.org/10.1016/j.dadm.2016.03.005

in older adults is currently unknown. The Department of Health and Human Services along with the American College of Sports Medicine and the American Heart Association recommends accumulating 150 minutes of moderate intensity, or 75 minutes of vigorous intensity, or an equivalent combination of moderate and vigorous physical activity (MVPA) per week to promote health in all adults [9,10]. The temporal lobes atrophy with age, and this atrophy can predict cognitive decline to AD [11]. Thus, the present study investigated temporal lobe volumetric differences between older adults strictly categorized as having met PAR and those who were insufficiently active.

2. Methods

2.1. Participants

Ninety-one older adults (ages 50–74 years) from the Wisconsin Registry for Alzheimer's Prevention (WRAP) cohort volunteered to participate. The WRAP is a longitudinal registry composed of more than 1500 cognitively healthy adults [12]. The sample for this study included a large proportion of participants at-risk for AD (78%); defined as possessing either a parental family history (FH) of AD (70%), and/or the apolipoprotein epsilon 4 allele (*APOE* ε4) (46%), which closely reflects the makeup of the WRAP cohort. Participants were determined to be cognitively healthy using the mini-mental state examination (MMSE $\geq$ 24), did not have any major medical conditions (e.g. neurological diseases, psychiatric disorders), and were deemed safe for neuroimaging procedures. The University of Wisconsin Institutional Review Board approved all study procedures, and informed consent was obtained from all participants.

2.2. Physical activity assessment

All participants wore a triaxial GT3X+ accelerometer (Actigraph, Pensacola, FL) on their hip for seven consecutive days. Participants were instructed to wear the device during all waking hours, with the exception of when showering, swimming, or bathing. Standard accelerometry inclusion criteria consisted of at least 10 hours of valid wear time per day for a minimum of three weekdays and one weekend day [13]. Accelerometer data (in 1-second epochs) were processed using the validated Sojourn-3 axis method which uses an artificial neural net to identify boundaries between activities of different intensities and to estimate metabolic equivalents (METs) for each bout [14]. To calculate minutes spent in different intensity categories of PA, estimated METs were determined for each bout interval and were then separated into PA categories accordingly: <1.5 METs = sedentary, 1.5–2.99 METs = light, 3–5.99 METs = moderate and >6 METs = vigorous. Consistent with current public health PAR, total minutes spent in MVPA in bouts of 10 minutes or greater were used to determine whether the participant met the 150 minutes of MVPA recommendation [9,10].

2.3. Neuroimaging protocol

Magnetic resonance images (MRIs) were acquired on a GE X750 Discovery 3.0-T scanner with an eight-channel phased array head coil (General Electric, Waukesha, WI). Three-dimensional T1-weighted inversion recovery prepared spoiled gradient echo (SPGR) anatomic sequences were collected using the following parameters: TI/TE/TR = 450 ms/3.2 ms/8.2 ms, flip angle = 12°, slice thickness = 1 mm no gap, field of view (FOV) = 256, matrix size = 256 × 256, yielding a voxel resolution of 1 mm × 1 mm × 1 mm. Temporal lobe regions of interest (ROIs) included superior, middle, inferior, temporal pole, hippocampus, parahippocampal, and entorhinal. These were derived from the T1 images using the Freesurfer image analysis suite, version 5.1.0 (http://surfer.nmr.mgh.harvard.edu/), with automated volumetric segmentation. Further technical processing details are described in previous publications [15,16]. All images were visually inspected and edited (if necessary) by trained personnel to ensure that they were accurately reconstructed and without topologic defects. A summary measure for each region of interest was derived by averaging the values from the right and left hemispheres and then expressed as a percentage of intracranial volume (ICV) to account for differences in overall head size.

2.4. Statistical analyses

Independent samples *t* tests compared demographic information between those who met PAR and those who did not. Bivariate correlations explored the associations between age and temporal lobe volume ROIs. A single multivariate analysis of covariance was conducted to determine differences in brain volume between groups, controlling for age and gender with the significance level (α) set at 0.05. Because there is evidence showing that PA may have a more robust effect on brain volume in those at-risk for AD [17], secondary analyses limited to at-risk participants were conducted. All analyses were conducted using IBM SPSS, version 22.0.

3. Results

3.1. Sample

Ninety-one cognitively healthy (MMSE = 29.3 ± 1.1) participants (mean age = 64 ± 5.8) completed the study (see Table 1 for participant characteristics). Twenty-nine participants met the PAR of 150 minutes of MVPA and sixty-two did not. Groups did not differ on any measured demographic characteristics ($P > .05$). The volumes of all ROIs included in the analyses were significantly and negatively correlated with age ($P < .05$; $r_{range} = -.173$ to $-.352$).

3.2. Physical activity and temporal lobe volume

After controlling for the effects of gender and age, there were significant group effects for the inferior temporal

Table 1
Participant demographics

Variable	Total sample	Sample meeting PAR	Sample not meeting PAR
Sample size	91	29	62
Female, %	66	62	68
Age, y	64.1 (5.8)	63.5 (4.9)	64.4 (6.2)
BMI, kg/m^2	28.1 (5.7)	26.5 (3.0)	28.9 (6.4)
Education, y	16.3 (2.4)	15.7 (2.5)	16.6 (2.3)
MMSE, score	29.3 (1.1)	29.3 (1.5)	29.2 (1.2)
At-risk, %	78	76	79
FH positive, %	70	69	71
APOE ε4 positive, %	46	34	52
Caucasian, %	96	93	97
Actigraph worn, d	6.5 (0.5)	6.5 (0.5)	6.5 (0.5)
MVPA, total minutes	109.9 (108.6)	243.8 (84.3)*	47.2 (40.3)

Abbreviations: BMI, body mass index; MMSE, mini-mental state examination; *APOE* ε4, the epsilon 4 allele of the apolipoprotein E gene; FH, family history; MVPA, moderate-vigorous physical activity counting toward recommendations.

Values indicate mean score and standard deviation, unless otherwise indicated.

*significant group difference ($P < .05$).

lobe (F(1,87) = 4.545, $P = .036$, $\eta^2_P = .050$) and the temporal pole (F(1,87) = 5.105, $P = .026$, $\eta^2_P = .055$). Individuals who met current PAR had larger inferior temporal and temporal pole volumes compared to those who did not meet PAR. No significant group differences were observed for the other ROIs ($P > .05$; Table 2). Limiting the sample to individuals at-risk (n = 22 met PAR; n = 49 did not meet PAR), we observed similar results with larger effect size differences specifically for the inferior temporal lobe [inferior temporal lobe: (F(1,67) = 6.820 $P = .011$, $\eta^2_P = .092$); temporal pole (F(1,67) = 4.258, $P = .043$, $\eta^2_P = .060$)].

4. Discussion

In this cohort of cognitively healthy older adults, we observed greater temporal lobe volume in participants who engaged in current recommended levels of PA compared to those who did not. The observed effect size for the inferior temporal lobe was strengthened when the sample was limited to at-risk participants, highlighting the importance of meeting PAR for individuals with familial and/or genetic risk for AD. Our findings suggest that participation in regular PA at or above recommended levels may mitigate the detrimental effects of aging on temporal lobe volume.

Physical activity and fitness have been associated with gray matter volume in older adults [6,7]; however, there is limited research investigating whether meeting PAR is effective for attenuating declines in brain volume. Okonkwo et al. [8] found individuals who self-reported being physically active experienced less age-related alterations in AD biomarkers, including hippocampal volume. Another study found that only individuals self-reporting high levels of PA participation (top quartile) had greater gray matter volume, including areas within the temporal lobe than individuals in the lower three quartiles. The lower three quartiles were not significantly different from each other, suggesting there may be a threshold of PA necessary to confer protection [18]. Given the inherent limitations of self-reported PA, this study provides stronger evidence that meeting PAR can protect brain volume [19].

In our sample, 32% met the weekly PAR which is higher than the reported national average of 5% of older adults [13]. This discrepancy highlights both a strength and a limitation of this study. The large percentage of individuals who met PAR allowed for meaningful comparisons between groups. However, the large percentage of participants meeting PAR suggests that the volunteer WRAP cohort may not be reflective of the general population of older adults.

Individuals at-risk for AD experience accelerated rates of brain atrophy. The findings of this study add to a growing body of literature supporting the positive impact of PA behaviors on brain health in older adulthood. However, the cross-sectional design of the present study does not allow for causal inferences to be made. Dose manipulation studies aimed at manipulating physical activity and determining whether a change in PA levels is necessary to preserve temporal lobe volume are needed to more fully test these hypotheses. Notably, using objective assessment of PA behaviors, this study suggests that weekly PA at or above PAR is not only beneficial for overall health; it may be an important way for older adults to preserve temporal lobe volume using natural, affordable methods that are safe and accessible.

Table 2
Temporal lobe volumes

Region of interest	Sample meeting PAR	Sample not meeting PAR	*P* value	Cohen's *d* effect size
Superior temporal	.5004 (.0380)	.4994 (.0462)	.946	.02
Middle temporal	.4407 (.0327)	.4376 (.0404)	.789	.08
Inferior temporal	.4615 (.0486)*	.4405 (.0418)	.036	.46
Temporal pole	.0609 (.0061)*	.0575 (.0068)	.026	.53
Hippocampus	.5714 (.0687)	.5746 (.0624)	.732	.05
Parahippocampal	.0977 (.0098)	.0976 (.0125)	.950	.01
Entorhinal	.0523 (.0104)	.0518 (.0075)	.852	.06

Values indicate mean volume and standard deviation. Region of interest volumes expressed as a % of ICV.

*significant group difference controlling for age and gender ($P < .05$).

Acknowledgments

This work was supported by the National Institute on Aging grants K23 AG045957 (O.C.O.), R01 AG031790 (C.M.C.), R01 AG021155 (S.C.J.), R01 AG027161 (S.C.J.), and P50 AG033514 (S.A.); and by a Clinical and Translational Science Award (UL1RR025011) to the University of Wisconsin, Madison. Portions of this research were supported by the Extendicare Foundation, the Alzheimer's Association, the Wisconsin Alumni Research Foundation, the Helen

Bader Foundation, Northwestern Mutual Foundation, and the Veterans Administration including facilities and resources at the Geriatric Research Education and Clinical Center of the William S. Middleton Memorial Veterans Hospital, Madison, WI. Jacob Meyer was supported by a National Research Service Award from the Health Resources and Services Administration T32HP10010 to the University of Wisconsin Department of Family Medicine and Community Health. We acknowledge WRAP psychometrists for their assistance with neuropsychological data collection, and the researchers and staff at the University of Wisconsin–Madison Waisman Center for help with brain imaging. Finally, we thank study participants in the Wisconsin Registry for Alzheimer's Prevention without whom this work would not be possible.

RESEARCH IN CONTEXT

1. Systematic review: The authors surveyed the literature related to fitness, physical activity (PA), and brain volume in older adults. There is evidence that fitness and self-reported PA are positively associated with brain volume in older adulthood. However, the influence of objectively meeting PA recommendations (via accelerometry) on brain volume in adults is currently unknown.
2. Interpretation: These findings support that regular engagement in PA at or above the current recommendations is not only beneficial for overall health, it may be an important way for older adults to preserve temporal lobe volume using natural, affordable methods that are safe and accessible.
3. Future directions: The analyses in the present study are cross-sectional therefore causal inferences cannot be made. Dose manipulation studies aimed at manipulating PA and determining whether a change in PA levels are necessary to preserve temporal lobe volume are needed to more fully test these hypotheses.

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