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Domains of physical activity and brain volumes: A population-based study

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ABSTRACT

Observational studies and intervention trials suggest that physical activity (PA) is beneficial for human brain morphology, especially in older individuals. Few population-based studies examined whether domain-specific PA is associated with brain volumes. Accordingly, we studied putative associations of PA during leisure time, sports and work with volumes of the hippocampus, the prefrontal cortex, the temporal lobe, gray matter (GM), white matter (WM) and total brain (TBV) after 5.9 years by applying volumetric analysis and voxel-based morphometry (VBM) with SPM 8/VBM 8 to brain magnetic resonance imaging data of 834 participants (447 women) aged 25 to 83 years from the population-based Study of Health in Pomerania. The Baecke questionnaire was used to assess domain-specific PA (Leisure time, Sport, and Work Index) at baseline. After correcting for multiple testing, volumetric analyses did not show any significant association of domain-specific PA and volumes of the hippocampus, the prefrontal cortex, the temporal lobe, GM, WM and TBV. Multivariable-adjusted VBM analyses of the associations between PA domains with GM and WM volumes did not reveal any statistically significant results. Region of interest analyses revealed a statistically significant cluster of increased GM volume in the bilateral anterior cingulate cortex in association with PA during sports. In conclusion, the overall results contrast with the findings from previous studies that found significant associations between PA and brain volumes. In addition, it remains unclear whether a differential association exists between domains of PA and brain volumes. Thus, future studies with larger sample size and prospective design are needed to investigate potential domain-specific associations of PA with brain volumes.

Introduction

Human aging is associated with structural brain changes such as a decrease of gray (GM) and white matter (WM) volume and integrity. However, rates and trajectories of change vary among individuals, brain regions, and structures (Raz et al., 2010). The rising prevalences of age-related cognitive impairment, Alzheimer's disease and other dementias are imposing a large burden on individuals, health systems, and economies (Prince et al., 2015). In the absence of an available curative treatment, it is crucial to identify modifiable protective factors that contribute to healthy brain aging. Physical activity (PA) is a modifiable lifestyle factor that seems to have beneficial effects on brain health. Findings from meta-analyses show that increased PA is associated with a reduced risk of cognitive decline and dementia (Bherer et al., 2013; Blondell et al., 2014) and with improved neurocognitive health (Stillman et al., 2016). Several observational

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(Demirakca et al., 2014; Erickson et al., 2010; Gow et al., 2012; Killgore et al., 2013) and intervention studies (Carlson et al., 2015; Colcombe et al., 2006; Erickson et al., 2011; Ruscheweyh et al., 2011) have investigated the association between PA and brain morphology. Although findings were not homogeneous, most studies showed that PA was associated with greater GM volumes in the prefrontal cortex and hippocampus in older adults (Erickson et al., 2014; Niemann et al., 2014). Findings from a recent meta-analysis suggest that PA is positively associated with WM volumes in older adults (Sexton et al., 2015).

Of the studies that investigated PA and brain morphology, the vast majority concentrated on adults aged 60 years and older, and only a limited number of studies investigated the relationship between PA and brain volumes at younger ages. Two studies among healthy younger and middle-aged adults found a positive association between self-reported PA and hippocampal volumes (Demirakca et al., 2014; Killgore et al., 2013). Thus, more evidence regarding the association between PA and brain volumes in younger age groups is needed to draw conclusions if PA during early and middle adulthood is beneficial for healthy brain aging. In addition, previous research focused mainly on a single domain such as leisure time PA (Erickson et al., 2014). However, leisure time PA constitutes only a small part of total daily activity, and does not show the overall picture of PA. PA typically occurs in various domains (i.e., recreational, household, transport, occupational). In addition, considering only one domain ignores activities undertaken in other domains, which could bias findings (Kyu et al., 2016).

It has been shown that higher levels of total and domain-specific leisure time and occupational PA are associated with reduced all-cause mortality (Samitz et al., 2011). Furthermore, PA during leisure time, transport and sport activities are inversely associated with mental ill-health, whereas work-related PA was positively associated to adverse mental health outcomes (White et al., 2017). Findings from a systematic review indicate that leisure time PA is protective against Alzheimer's disease, whereas work-related PA is not (Stephen et al., 2017). So far, only one study with a relatively small sample size has investigated domain-specific associations of PA and brain volumes in healthy younger and middle-aged adults (Demirakca et al., 2014). We hypothesized that PA during leisure time, sport and at work is positively associated with volumes of the hippocampus, the prefrontal cortex, the temporal lobe, GM, WM, and total brain volumes (TBV). We performed volumetric analyses and analyses using voxel-based morphometry (VBM) to explore the relationship between domains of PA and brain volumes. Furthermore, we conducted region of interest (ROI) analyses of brain areas known to be associated with physical activity, such as the hippocampus, the prefrontal cortex, the cingulate cortex, the basal ganglia, and the temporal cortex (Erickson et al., 2014).

Material and methods

Sample

SHIP is a prospective population-based cohort of adults from West Pomerania, a north-eastern region in Germany (Volzke et al., 2011). A stratified cluster-random sample of 6265 eligible individuals was drawn from local population registries and 4308 (2192 women) participated in the first examination (SHIP-0) between 1997 and 2001 (response of 69%). A second examination cycle (SHIP-1) was conducted between 2002 and 2006 and comprised 3300 participants. PA was determined in 3255 participants at SHIP-1 (1517 for work-related PA) (Volzke et al., 2011). This examination cycle was, therefore, defined as the baseline examination for the present analyses. From the second follow-up examination (SHIP-2; 2008 to 2012), 2333 subjects were invited to undergo whole-body magnetic resonance imaging (MRI). After exclusion of subjects who refused to participate or who fulfilled exclusion criteria for MRI (e.g., cardiac pacemakers, pregnancy), 1182 subjects from SHIP-2 underwent MRI scanning (Hegenscheid et al., 2013). We restricted the analyses to participants without cerebrovascular pathologies that might affect brain volumes (a list of these conditions is provided in supplementary Table S1; exclusions n= 239). The analytic cohort comprised 834 individuals (447 women) with complete baseline and follow-up information. We further conducted VBM analyses on a subsample of the data with even stricter quality control. For the VBM, we further excluded subjects due to medical conditions (e.g., a history of cerebral tumor, stroke, Parkinson's diseases, multiple sclerosis, epilepsy, hydrocephalus, enlarged ventricles, pathological lesions) or technical reasons (e.g., severe movement artifacts or inhomogeneity of the magnetic field). Additionally, we performed the homogeneity check of the GM images as implemented in the VBM 8 toolbox and excluded extreme outliers which left us with a sample of N=778 (leisure time or sport index VBM) and N=511 (work index VBM). All participants gave written informed consent and the Ethics Committee of the University of Greifswald approved the study protocol.

Measurement of brain volumes

At follow-up, all participants were scanned with a 1.5-tesla MRI (MAGNETOM Avanto; Siemens Healthcare, Erlangen, Germany) with a T1-weighted magnetization prepared rapid acquisition gradient-echo (MPRAGE) sequence and the following parameters: axial plane, repetition time = 1900 ms, echo time = 3.4 ms, flip angle = 15°, and original resolution of 1.0 mm^3 x 1.0 mm^3 x 1.0 mm^3 image processing. (Van der Auwera et al., 2015) Images were analyzed using the fully automated and validated segmentation software FreeSurfer 5.1 (Fischl et al., 2002; Schmaal et al., 2015). Here, we investigated volumes of the hippocampus, the prefrontal cortex, the temporal lobe, as well as total brain GM, WM, and TBV. TBV was generated from the sum of left hemisphere cortical WM volume, right hemisphere cortical WM volume, and total GM volume.

Assessment of PA

At baseline, PA was assessed using the Baecke questionnaire (Baecke et al., 1982) during a computer-assisted interview. The questionnaire consists of 16 items organized in three sections: PA at work, sport during leisure time and PA during leisure time excluding sport, scored on a five-point Likert scale, ranging from never to always or very often. The leisure time domain describes physical activities such as walking or cycling during leisure time and the corresponding time spent with these activities. Similarly, the sports domain includes information on the types of sport and the time dedicated to that type of sport. The work domain encompasses the intensity of physical activity at work. The three derived indices are scored in arbitrary units ranging from 1 to 5. In this report, we refer to Leisure time Index, Sport Index, and Work Index. The Baecke questionnaire has been used in a number of studies in various populations; retest reliability ranges between 0.65 and 0.92 (Florindo and de Oliveira Latorre, 2003; Pols et al., 1995; Richardson et al., 1995), and the correlation with doubly labeled water is high (0.69) (Philippaerts et al., 1999). A matrix of Pearson coefficients for the three activity indices derived from the Baecke index is provided in supplementary Table S2.

Covariates

At baseline, income was 'equalized' by dividing the household income (in €) by the square root of the number of household members. Smoking was grouped into never, former or current smoking. Alcohol consumption (in grams per day, g/d) was derived from a beverage-specific quantity-frequency index (Markus et al., 2015). Education, blood pressure, total cholesterol, high-density lipoprotein (HDL) cholesterol, and HbA1c were determined as previously described (Markus et al., 2015).