Neurobiology of Aging 34 (2013) 83–90

NEUROBIOLOGY OF AGING

www.elsevier.com/locate/neuaging

Association between physical activity and brain health in older adults

Christian Benedict[a,*], Samantha J. Brooks[a], Joel Kullberg[b], Richard Nordenskjöld[b], Jonathan Burgos[a], Madeleine Le Grevès[a], Lena Kilander[c], Elna-Marie Larsson[b], Lars Johansson[b], Håkan Ahlström[b], Lars Lind[d], Helgi B. Schiöth[a]

[a] *Uppsala University, Department of Neuroscience, Uppsala, Sweden*
[b] *Uppsala University, Department of Radiology, Uppsala, Sweden*
[c] *Uppsala University, Department of Public Health and Caring Sciences/Geriatrics, Uppsala, Sweden*
[d] *Uppsala University, Department of Medical Sciences, Uppsala, Sweden*

Received 30 December 2011; received in revised form 19 April 2012; accepted 24 April 2012

Abstract

In the present cross-sectional study, we examined physical activity (PA) and its possible association with cognitive skills and brain structure in 331 cognitively healthy elderly. Based on the number of self-reported light and hard activities for at least 30 minutes per week, participants were assigned to 4 groups representing different levels of PA. The cognitive skills were assessed by the Mini Mental State Examination score, a verbal fluency task, and the Trail-making test as a measure of visuospatial orientation ability. Participants also underwent a magnetic resonance imaging of the brain. Multiple regression analysis revealed that greater PA was associated with a shorter time to complete the Trail-making test, and higher levels of verbal fluency. Further, the level of self-reported PA was positively correlated with brain volume, white matter, as well as a parietal lobe gray matter volume, situated bilaterally at the precuneus. These present cross-sectional results indicate that PA is a lifestyle factor that is linked to brain structure and function in late life.

Keywords: Physical activity; Brain morphometry; Cognitive function; Elderly

1. Introduction

Lifespan in modern societies has significantly increased in the last few decades. As a result, cognitive frailty is emerging as 1 of the greatest health threats of the twenty-first century as aging underlies cognitive decline and development of dementia. Although evidence links age-related cognitive decline with genetic factors (Benedict et al., 2011; Ho et al., 2010; Keller et al., 2010), the dynamics of brain aging seems to be sensitive to lifestyle modification (Bishop et al., 2010). One lifestyle component that is assumed to slow the rate of cognitive aging is physical activity (PA) (Richards et al., 2003; Singh-Manoux et al., 2005). Studies in humans have shown that those who are physically active perform better on global, logic-based, verbal, and visuospatial cognitive tests, and have reduced risk of developing Alzheimer's disease (AD) compared with those who are more adherent to a sedentary lifestyle (Aberg et al., 2009; Geda et al., 2010; Kramer et al., 1999; Larson et al., 2006; Rovio et al., 2005). Adding further evidence that PA slows brain aging, both observational and interventional studies have shown that elderly who are more physically active have significantly greater brain volumes situated in temporal brain regions including the hippocampus and entorhinal cortex, compared with less active adults (Colcombe et al., 2003; Erickson et al., 2009, 2010, 2011; Ho et al., 2011). These findings support the view that high PA during late adulthood could serve as a promising public health intervention to counteract cognitive decline and brain matter loss facing aging modern societies. However, a potential drawback of many studies is the inclusion of participants with heterogeneous age. For instance, with regard to decreasing

* Corresponding author at: University of Uppsala, Department of Neuroscience (Medical faculty), Box 593, Husargatan 3, Uppsala, Sweden. Tel.: +46 18 471 4136; fax: +46 18 51 1540.
E-mail address: christian.benedict@neuro.uu.se (C. Benedict).

0197-4580/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neurobiolaging.2012.04.013

muscle mass across the lifespan, it is likely that the maintenance of a certain PA level becomes more difficult with advancing age (Hawkins et al., 2003).

Against this background, we aimed to examine the association between self-reported PA and both cognitive performance and brain morphometry in 331 cognitively healthy elderly. During assessment of these variables, all participants were at the age of 75 years. It was hypothesized that higher levels of self-reported PA would be linked to a greater global gray matter volume and higher scores on the cognitive tests, and vice versa. Additionally, based on previous findings from the cardiovascular Health Cognition Study (Erickson et al., 2010), we hypothesized that PA would be linked to greater regional gray matter volumes situated in the left precentral gyrus, bilateral supplementary motor area, bilateral precuneus, and bilateral hippocampus.

2. Methods

2.1. Study population and design

The Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) started in 2001. The primary study aim was to investigate endothelial function and arterial compliance in a random sample of elderly subjects (Lind et al., 2005). In 2003, the enrollment of participants was finished, and the cohort included 1016 (50% female) individuals at the age of 70 years. Between 2006 and 2008, 827 subjects from the initial cohort agreed to participate in a follow-up investigation (81.4% response rate), i.e., when they were 75 years old. In addition to the major measurements (e.g., endothelial function and arterial compliance), subjects' self-reported physical activity was monitored by standardized questionnaires, and cognitive skills were assessed. Of the individuals who were reinvestigated at the age of 75 years, a subsample of 409 elderly was assigned to a magnetic resonance imaging (MRI) session (49.5% of the cohort that was reinvestigated at the age of 75 years). Note that only a subsample was chosen, due to time and cost constraints. Of this number, 331 elderly (including 164 females and 46 diabetes mellitus patients) satisfied all criteria for this study, including cognitively normal clinical status (identified by an Mini Mental State Examination [MMSE] score greater than 26) (Folstein et al., 1975), absence of strokes or neurologic diseases (e.g., tumors) at ages 70 and 75, and valid measures from the MRI brain scan (flowchart, see Fig. 1). Exclusions were administered to minimize the confounding effects of variables related to our main question: does self-reported physical activity relate to cognition and brain structure among cognitively healthy elderly.

The study was approved by the Ethics Committee of Uppsala University, Faculty of Medicine. All participants gave their written informed consent.

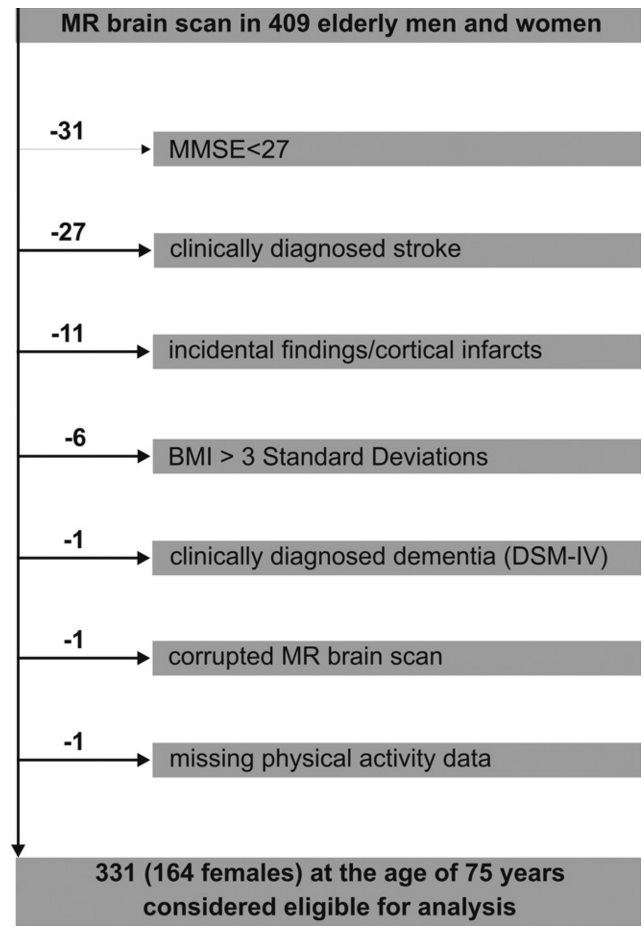

Fig. 1. Subject inclusionary criteria and sa mple sizes. Initially, 1016 individuals (509 females) were examined at the age of 70 years. From these individuals, 409 agreed to participate in a magnetic resonance imaging (MRI) whole brain scan at the age of 75 years. To ensure a cognitively healthy population, those with a history of dementia or stroke, those with a body mass index (BMI) $>$ 3 standard deviations, those with pathological lesions on MRI (including arachnoidal cyst, bilateral hygromas, meningiomas, and schwannoma), those whose physical activity data were missing, and those who scored less than 27 on the Mini Mental State Examination (MMSE) to control for mild cognitive impairment were excluded. Furthermore, we examined each individual's MRI scan, and we excluded 1 that was affected by movement artifacts. Thus, 331 elderly men and women were considered eligible to analyze the association between the self-reported physical activity, cognitive functions, and gray matter volume at the age of 75 years.

2.2. Assessment of physical activity and cognitive skills

PA was divided into light and hard exercise and classified as the number of activities with a duration of at least 30 minutes per week. The participants were asked how many times per week they performed light (e.g., walking, gardening) or hard exercise (e.g., running, swimming) for at least 30 minutes. Based on the responses to these questions, 4 PA categories were constructed: very low, low, medium, and high (Table 1). The questions used here to assess PA have been validated elsewhere (Michaëlsson et al., 2007).

Cognitive measurements included the MMSE to ascertain the overall cognitive status (Folstein et al., 1975), a