Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

Brain Research

Research Report

Cardiorespiratory fitness and brain diffusion tensor imaging in adults over 80 years of age

Qu Tian[a,*], Eleanor M. Simonsick[b], Kirk I. Erickson[c], Howard J. Aizenstein[d], Nancy W. Glynn[a], Robert M. Boudreau[a], Anne B. Newman[a], Stephen B. Kritchevsky[e], Kristine Yaffe[f], Tamara Harris[g], Caterina Rosano[a], for the Health ABC study

[a]Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA, USA
[b]Intramural Research Program, National Institute on Aging, Baltimore, MD 21225, USA
[c]Department of Psychology, University of Pittsburgh, Pittsburgh, PA 15260, USA
[d]Departments of Psychiatry, Bioengineering, and Clinical and Translational Science, University of Pittsburgh, Pittsburgh, PA 15213, USA
[e]Sticht Center on Aging, Section on Gerontology and Geriatric, Medicine, Wake Forest School of Medicine, Winston-Salem, NC, USA
[f]Departments of Psychiatry, Neurology and Epidemiology, University of California, San Francisco, San Francisco, CA 94121, USA
[g]Intramural Research Program, Laboratory of Epidemiology, Demography, and Biometry, National Institute on Aging, Bethesda, MD, USA

ARTICLE INFO

Article history:
Accepted 1 September 2014
Available online 6 September 2014

Keywords:
Cardiorespiratory fitness
Diffusion tensor imaging
Microstructural integrity
Very old adults
Neuroepidemiology

ABSTRACT

A positive association between cardiorespiratory fitness (CRF) and white matter integrity has been consistently reported in older adults. However, it is unknown whether this association exists in adults over 80 with a range of chronic disease conditions and low physical activity participation, which can influence both CRF and brain health. This study examined whether higher CRF was associated with greater microstructural integrity of gray and white matter in areas related to memory and information processing in adults over 80 and examined moderating effects of chronic diseases and physical activity. CRF was measured as time to walk 400 m as quickly as possible with concurrent 3 T diffusion tensor imaging in 164 participants (57.1% female, 40.3% black). Fractional anisotropy (FA) was computed for cingulum, uncinate and superior longitudinal fasciculi. Mean diffusivity (MD) was computed for dorsolateral prefrontal cortex, hippocampus, parahippocampus, and entorhinal cortex. Moderating effects were tested using hierarchical regression models. Higher CRF was associated with higher FA in cingulum and lower MD in hippocampus and entorhinal cortex (β, sex-adjusted p: −0.182, 0.019; 0.165, 0.035; and 0.220, 0.006, respectively). Hypertension attenuated the association with MD in entorhinal cortex. Moderating effects of chronic diseases and physical activity in walking and climbing stairs on these associations were not significant. The association of higher CRF with greater microstructural integrity in selected subcortical areas appears robust, even among very old adults

*Corresponding author. 251 Bayview Blvd., Suite 100, Room 04B316, Baltimore, MD 21224, USA. Fax: +1 410 558 8674.
E-mail address: qu.tian@nih.gov (Q. Tian).

http://dx.doi.org/10.1016/j.brainres.2014.09.003
0006-8993/

with a range of chronic diseases. Intervention studies should investigate whether increasing CRF can preserve memory and information processing by improving microstructure and potential effects of hypertension management.

1. Introduction

Cumulative evidence suggests higher cardiorespiratory fitness (CFR) is associated with improved cognitive function in older adults (for meta-analysis, see Colcombe and Kramer, 2003; for review, see Kramer et al., 2005, 2006). However, neuroimaging evidence of the mechanisms underlying the neuroprotective effect of CRF is sparse, especially at the microstructural level. Most neuroimaging studies have focused on macrostructure of the brain and have found that higher CRF is associated with fewer white matter (WM) lesions (Sen et al., 2012) and greater brain volume, mostly localized in prefrontal cortex and medial temporal lobe (MTL) among cognitively healthy adults in their mid-sixties (Alosco et al., 2013; Colcombe et al., 2003, 2006; Erickson et al., 2009, 2011; McAuley et al., 2011; Weinstein et al., 2012). These regions support executive control function and memory (Park et al., 2001) and are highly susceptible to changes in blood oxygenation levels (Bladin et al., 1993).

However, few studies have examined the association between CRF and microstructural integrity. Diffusion tensor imaging (DTI) provides accurate measures of brain parenchyma microstructure and can also indicate early stages of cognitive impairment (Sasson et al., 2013). Disruption of WM integrity is frequently observed as decreased fractional anisotropy (FA) (Alexander et al., 2007), while increased mean diffusivity (MD) suggests the loss of microstructural integrity in gray matter (GM) (Whitwell et al., 2010). Among the few studies focusing on parenchymal microstructure, DTI was applied to examine WM only in relatively young and well-functioning older adults (Johnson et al., 2012; Marks et al., 2007, 2011; Tseng et al., 2013) and in patients with multiple sclerosis (Voss et al., 2010). Overall, results indicated a positive association between CRF and WM integrity in corpus callosum, cingulum, and uncinate fasciculus. One small intervention study reported increases in fitness from walking were associated with greater WM integrity in prefrontal, parietal, and temporal regions in well-functioning older adults (Voss et al., 2012). However, the microstructural integrity of GM in relation to CRF has not been examined. Examining the spatial distribution of the microstructure in both WM and GM can further the understanding of the neuroprotective effects of CRF.

It is also unclear whether CRF would have a neuroprotective effect in very old adults who are living with chronic disease conditions and low physical activity participation. This is important, because chronic disease and physical activity could affect both CRF and brain health. For example, chronic diseases may lower CRF levels directly or indirectly through limited physical activity participation. Previous investigations have not examined the contribution of chronic disease or physical activity to the neuroprotective effects of higher CRF. It is important to quantify the association between CRF and structural integrity of the brain in the context of chronic diseases and physical activity participation, in order to identify the optimal CRF level for preserving brain health in older age.

One challenge in examining the relationship between CRF and brain health in very old age is the limited availability of safe and accurate measures of CRF. Most prior studies focusing on well-functioning adults in their mid-sixties to seventies applied the graded maximal exercise test (Colcombe et al., 2003; Erickson et al., 2009; Johnson et al., 2012; Marks et al., 2011) which can pose safety risks for adults over 80 years of age (Hollenberg et al., 1998; Wilson et al., 1986). By contrast, the self-paced 400-m long-distance corridor walk test has high safety in measuring CRF and it has been previously validated against the graded maximal exercise test (Simonsick et al., 2006). The 400-m walk time is shown to be a valid indicator of CRF in adults aged 60 and older, which is highly correlated with peak VO_2 and explains 75.5% of the variance of peak VO_2 (Simonsick et al., 2006).

This study examined the cross-sectional association between CRF, measured as time to complete the 400-m walk as quickly as possible (Simonsick et al., 2006), and neuroimaging markers of microstructural integrity of WM and GM in a cohort of adults over 80 years of age, while accounting for chronic diseases and physical activity. It was hypothesized that higher CRF would be associated with greater brain integrity in prefrontal cortex and MTL because of their localizations within watershed areas and their known associations with memory (Erickson et al., 2011; McAuley et al., 2011) and processing speed (Spirduso, 1980). It was also hypothesized that these associations would be moderated by higher burden of prevalent diseases and lower physical activity levels.

2. Results

Demographic characteristics of the 164 participants who completed the 400-m walk test and had DTI data in 2006–2008 (51.8% female, 40.3% black as shown in Table 1) were similar to those who completed the 400-m walk test in the parent cohort at study entry (48.8% female, 37.7% black) (Newman et al., 2006). Compared to those who received a brain Magnetic Resonance Imaging (MRI) but did not complete the 400-m walk test ($n=62$), these 164 completers were more likely to be men ($p=0.016$) and had higher digit symbol substitution test (DSST) score ($p=0.019$), faster gait speed ($p<0.001$), and lower body mass index (BMI) ($p=0.016$). The 164 completers also tended to have lower prevalence of