NeuroImage 146 (2017) 1084–1092

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Cardiorespiratory fitness is differentially associated with cortical thickness in young and older adults

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ARTICLE INFO

Keywords:
Aerobic fitness
Physical activity
Lifespan
Aging
Brain maintenance
MRI

ABSTRACT

Aging is associated with reductions in gray matter volume and cortical thickness. One factor that may play a role in mitigating age-associated brain decline is cardiorespiratory fitness (CRF). Although previous work has identified a positive association between CRF and gray matter volume, the relationship between CRF and cortical thickness, which serves as a more sensitive indicator of gray matter integrity, has yet to be assessed in healthy young and older adults. To address this gap in the literature, 32 young and 29 older adults completed treadmill-based progressive maximal exercise testing to assess CRF (peak VO_2), and structural magnetic resonance imaging (MRI) to determine vertex-wise surface-based cortical thickness metrics. Results indicated a significant CRF by age group interaction such that Peak VO_2 was associated with thicker cortex in older adults but with thinner cortex in young adults. Notably, the majority of regions demonstrating a positive association between peak VO_2 and cortical thickness in older adults overlapped with brain regions showing significant age-related cortical thinning. Further, when older adults were categorized as high or low fit based on normative data, we observed a stepwise pattern whereby cortex was thickest in young adults, intermediate in high fit older adults and thinnest in low fit older adults. Overall, these results support the notion that CRF-related neuroplasticity may reduce although not eliminate age-related cortical atrophy.

1. Introduction

Cerebral volume loss is a well-documented correlate of the aging process, accompanied by a reliable pattern of regional cortical thinning with advancing age (Fjell et al., 2009b; Salat et al., 2004; Shaw et al., 2016). Brain regions most susceptible to age-related cortical degeneration largely coincide with heteromodal association areas that support higher-level processing, and include lateral temporal, inferior parietal, and frontal regions, as well as the precuneus, temporoparietal junction, and fusiform gyrus (Fjell et al., 2009a, 2009b; Shaw et al., 2016). Despite a general trend of cortical atrophy in healthy aging, individual differences have been observed in the rate and extent of degeneration, with some adults maintaining relatively more intact structural integrity throughout late life than same-aged peers (Pfefferbaum and Sullivan, 2015). Thus, in an effort to promote optimal brain health within a society where the population distribution is increasingly shifting towards older ages (Vincent and Velkoff, 2010), identifying relevant lifestyle factors that may protect against age-related neurostructural decline is warranted.

One factor that may play a role in mitigating age-associated brain decline is cardiorespiratory fitness[1] (CRF). CRF reflects the efficiency of the circulatory and respiratory systems to provide oxygenated blood to musculature during sustained aerobic physical activity. As a modifiable health factor, CRF can be optimized through regular engagement in

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[1] cardiorespiratory fitness (CRF); low fit older adult (LFOA) high fit older adult (HFOA); young adult (YA); older adult (OA); American College of Sports Medicine (ACSM); Wechsler Test of Adult Reading (WTAR); Montreal Cognitive Assessment (MoCA); Center for Epidemiologic Studies Depression Scale (CES-D); body mass index (BMI).

http://dx.doi.org/10.1016/j.neuroimage.2016.10.033
Received 14 July 2016; Accepted 20 October 2016
Available online 28 October 2016
1053-8119/ Published by Elsevier Inc.

physical activity of moderate to vigorous intensity such as jogging, swimming, or biking. The gold standard of CRF assessment is treadmill-based graded maximal exercise testing, which yields a measure of peak volume of oxygen consumption (peak VO_2) at maximum intensity exercise. Compared to self-report or estimated CRF metrics, peak VO_2 provides an objective and reliable indicator of CRF. Whereas systemic benefits of enhanced CRF to both emotional and physical health are well documented (DiLorenzo et al., 1999; Myers et al., 2015; Papasavvas et al., 2016; Tozzi et al., 2016; Warburton et al., 2006), only recently have studies begun to explore the relation between CRF and brain structure, particularly in the context of aging.

Cross-sectional studies of older adults have generally reported a positive association of CRF with gray matter volume (Boots et al., 2015; Bugg and Head, 2011; Erickson et al., 2007; Gordon et al., 2008; Weinstein et al., 2012) as well as with cognitive performance in the domains of executive function and memory (Barnes et al., 2003; Hayes et al., 2016). Interestingly, reliable CRF effects have been observed primarily within lateral prefrontal and parietal gray matter regions (Erickson et al., 2014; Hayes et al., 2014), cortical areas most vulnerable to age-related atrophy (Fjell et al., 2009b). Given this apparent regional overlap between CRF and aging effects, it follows that enhanced CRF could lessen the degree of cortical decline in aging. In support of this concept, aerobic exercise intervention studies have provided evidence of CRF-related neuroplasticity, as exercising older adults show greater regional brain volume than age-matched controls (Colcombe et al., 2006; Erickson et al., 2011).

Although positive associations between CRF and gray matter volume have been previously reported, it is less clear how CRF may relate to cortical thickness in older adult populations. Given that the surface area component used to define volume captures additional variance related to head size and the degree of regional cortical folding, volumetric approaches have been shown to yield less sensitive estimates of age-associated cortical atrophy when compared to surface-based cortical thickness techniques (Hutton et al., 2009; Lemaitre et al., 2012; Panizzon et al., 2009). Studies of patient populations (mild cognitive impairment, heart failure, and schizophrenia) have demonstrated positive associations between cortical thickness and CRF (Alosco et al., 2013; Reiter et al., 2015; Scheewe et al., 2013), yet the association between CRF and cortical thickness in the context of healthy aging remains unknown. One recent study (Lee et al., 2016) demonstrated a positive relation between self-reported physical activity and cortical thickness in healthy older adults. However, given that subjective CRF measures do not align well with objectively quantified peak VO_2 (Tager et al., 1998), additional study is warranted.

In the current cross-sectional study, we investigated age-dependent associations between objectively quantified CRF (peak VO_2) and cortical thickness in healthy older and young adults using a whole-brain cortical surface-based approach. The primary goals of this study were 1) to assess whether CRF is differentially associated with cortical thickness in young and older adults, 2) to determine the spatial overlap between observed CRF and aging effects across the cortex, and 3) to examine whether higher CRF in late life may eliminate age-related cortical thickness decline. Based on the previously reported beneficial effects of CRF on gray matter volume in aging, as well as positive associations between cortical thickness and CRF in patient populations, we expected to observe similar positive associations between CRF and cortical thickness in our older adult cohort. In particular, we anticipated that regions where CRF is positively associated with cortical thickness in older adults would overlap with frontal and temporoparietal regions most susceptible to age-related cortical thinning. Given the dearth of studies in young adults, we had no strong prediction about the association between CRF and cortical thickness for this cohort. A recent study of early adolescents (aged 9–11 years) found that greater CRF was associated with thinner cortex within regions of superior frontal, superior temporal and lateral occipital cortex (Chaddock-Heyman et al., 2015), a finding that likely reflects successful maturational development and neural pruning. The fact that in some brain regions protracted maturational cortical thinning has been observed throughout young adulthood (Tamnes et al., 2013) raises the possibility that young adults may show a negative association between CRF and cortical thickness similar to that observed in adolescents. By examining young and older adults in the same study, we were able to directly assess age-dependent associations between CRF and cortical thickness, and additionally, whether age-related differences in cortical thickness are impacted by CRF.

Table 1
Characteristics (mean and standard deviation) of young and older adults, as well as high fit (ACSM percentile ≥50) and low fit (ACSM percentile < 50) older adults.

	YA	OA	LFOA	HFOA
Number of participants	32 (17 F)	29 (15 F)	14 (6 F)	15 (9 F)
Age (years)	21.0 (3.1)[a]	63.7 (6.5)	64.8 (7.0)[b]	62.7 (6.1)[b]
Race (% Caucasian)	75 [a]	89	92 [a]	87[a]
Education (years)	14.4 (1.8)[a]	16.3 (2.6)*	15.4 (2.7)[a]	17.1 (2.4)[b]
WTAR (raw score)	43.2 (4.0)[a]	42.5 (6.2)	39.6 (6.5)[b]	45.2 (4.6)[a]
WTAR (standard score)	117.5 (6.6)[a]	115.0 (9.3)	110.6 (9.8)[b]	119.1 (6.8)[a]
MoCA	28.5 (1.5)[a]	27.8 (1.8)	26.9 (2.1)[b]	28.5 (1.0)[a]
CES-D	6.2 (4.1)[a]	5.2 (4.3)	5.0 (4.3)[a]	5.3 (4.5)[a]
BMI (kg/m^2)	23.0 (2.9)[a]	25.9 (4.5)*	28.4 (5.0)[b]	23.5 (2.2)[a]
Peak VO_2 (ml/kg/min)	39.0 (7.1)[a]	30.4 (7.4)*	24.9 (4.7)[b]	35.6 (5.4)[a]
Peak VO_2 ACSM percentile	35.9 (25.8)[a]	42.1 (31.7)	13.6 (16.0)[b]	68.7 (14.1)[c]
RER (VCO_2/VO_2)	1.26 (0.02)[a]	1.16 (0.08)*	1.15 (0.03)[b]	1.16 (0.02)[b]

Identical alphabetic superscripts denote the groups did not differ on this measure. American College of Sports Medicine (ACSM); Center for Epidemiological Studies Depression Scale (CES-D); Female (F); High Fit Older Adults (HFOA); Low Fit Older Adults (LFOA); Montreal Cognitive Assessment (MoCA); Older Adults (OA); Respiratory Exchange Ratio (RER); Wechsler Test of Adult Reading (WTAR); Young Adults (YA).
* Significant difference between YA and OA ($p < 0.05$).

2. Material and methods

2.1. Participants

Thirty-four young adults and 35 older adults were enrolled in the current study. Six older adults (four with incidental findings on MRI and two with excessive head motion) and two young adults (one with excessive head motion, the other whose peak VO_2 value was a statistical outlier at greater than 3 standard deviations above the mean) were excluded from the current analyses. The final sample consisted of 32 young adults (age=18–31 years) and 29 older adults (age=55–82 years; see Table 1 for participant characteristics).

To ensure our sample represented a wide range of cardiorespiratory fitness levels, participants were recruited from general participant pools (Boston University for young adults, and the Boston University Memory Disorders Research Center at VA Boston, Boston University Alzheimer's Disease Center, the Massachusetts Alzheimer's Disease Research Center, and the Alzheimer's Association TrialMatch for older adults) as well as through local libraries, YMCAs, and track (running) meets. Participants included in the study obtained at least a 12^{th} grade education, were free from contraindications to cardiopulmonary testing or Magnetic Resonance Imaging (MRI), and did not have major medical (e.g., myocardial infarction, vascular disease), neurological (e.g., Alzheimer's disease, Parkinson's disease, multiple sclerosis, head trauma), psychiatric (e.g., bipolar disorder, schizophrenia), or substance abuse issues that might affect cognition, as determined by a comprehensive health screen. Participants were screened for depression using a cut-off score of 16 on the Center for Epidemiologic Studies Depression Scale (CES-D) 20-item version. Mental status was assessed using the Montreal Cognitive Assessment (MOCA; http://www.mocatest.org/), where participants were excluded for cognitive