Neurobiology of Aging xxx (2014) 1–11

Contents lists available at ScienceDirect

Neurobiology of Aging

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

Hearts and minds: linking vascular rigidity and aerobic fitness with cognitive aging

Claudine Joëlle Gauthier [a,b,c,*], Muriel Lefort [d], Saïd Mekary [b,e], Laurence Desjardins-Crépeau [b,f], Arnold Skimminge [g], Pernille Iversen [g], Cécile Madjar [b,h], Michèle Desjardins [d,i,j], Frédéric Lesage [d,i], Ellen Garde [g], Frédérique Frouin [d], Louis Bherer [b,f,k], Richard D. Hoge [a,b]

[a] Department of Physiology/Biomedical Engineering, Université de Montréal, Montreal, Canada
[b] CRIUGM, Montreal, Canada
[c] Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany
[d] Sorbonne Universités UPMC Paris 06, CNRS, INSERM, LIB, Paris, France
[e] Department of Kinesiology, Université de Montréal, Montreal, Canada
[f] Psychology Department, UQAM, Montreal, Canada
[g] Danish Research Centre for Magnetic Resonance, Centre for Functional and Diagnostic Imaging and Research, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark
[h] Douglas Hospital/MNI, McGill University, Institut de Génie Biomédical, Montreal, Canada
[i] Départment de Génie Électrique, École Polytechnique de Montréal, Montréal, Canada
[j] Montreal Heart Institute, Montreal, Canada
[k] PERFORM, Concordia University, Montreal, Canada

ARTICLE INFO

Article history:
Received 26 April 2014
Received in revised form 18 July 2014
Accepted 15 August 2014

Keywords:
Healthy aging
Executive functions
Cardiorespiratory fitness
Aortic rigidity
Cerebrovascular function
Cerebrovascular reactivity
VO_2 max
Stroop

ABSTRACT

Human aging is accompanied by both vascular and cognitive changes. Although arteries throughout the body are known to become stiffer with age, this vessel hardening is believed to start at the level of the aorta and progress to other organs, including the brain. Progression of this vascular impairment may contribute to cognitive changes that arise with a similar time course during aging. Conversely, it has been proposed that regular exercise plays a protective role, attenuating the impact of age on vascular and metabolic physiology. Here, the impact of vascular degradation in the absence of disease was investigated within 2 groups of healthy younger and older adults. Age-related changes in executive function, elasticity of the aortic arch, cardiorespiratory fitness, and cerebrovascular reactivity were quantified, as well as the association between these parameters within the older group. In the cohort studied, older adults exhibited a decline in executive functions, measured as a slower performance in a modified Stroop task (1247.90 ± 204.50 vs. 898.20 ± 211.10 ms on the inhibition and/or switching component, respectively) than younger adults. Older participants also showed higher aortic pulse wave velocity (8.98 ± 3.56 vs. 3.95 ± 0.82 m/s, respectively) and lower VO_2 max (29.04 ± 6.92 vs. 42.32 ± 7.31 mL O_2/kg/min, respectively) than younger adults. Within the older group, faster performance of the modified Stroop task was associated with preserved aortic elasticity (lower aortic pulse wave velocity; $p = 0.046$) and higher cardiorespiratory fitness (VO_2 max; $p = 0.036$). Furthermore, VO_2 max was found to be negatively associated with blood oxygenation level dependent cerebrovascular reactivity to CO_2 in frontal regions involved in the task ($p = 0.038$) but positively associated with cerebrovascular reactivity in periventricular watershed regions and within the postcentral gyrus. Overall, the results of this study support the hypothesis that cognitive status in aging is linked to vascular health, and that preservation of vessel elasticity may be one of the key mechanisms by which physical exercise helps to alleviate cognitive aging.

1. Introduction

Aging is associated with decreased performance across a variety of cognitive domains, and executive functions are thought to be

* Corresponding author at: Neurology Department, Max Planck Institute for Human Cognitive and Brain Sciences, Stephanstrasse 1a, 04103 Leipzig, Germany. Tel.: +49 341 9940 2440; fax: +49 (0) 341 9940 104.
E-mail address: cgauthier@cbs.mpg.de (C.J. Gauthier).

0197-4580/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neurobiolaging.2014.08.018

particularly affected (Park and Reuter-Lorenz, 2009). The physiological changes underlying this decline are still under investigation, but studies have shown that markers of poor vascular health are associated with decreased cognitive performance (Bos et al., 2012; Brown et al., 2010; Girouard and Iadecola, 2006; Kearney-Schwartz et al., 2009; Mitchell et al., 2011; Zhong et al., 2014). There is therefore much to gain from understanding the link between age-related cognitive decline and declining vascular health, as well as the influence of modulating factors such as cardiorespiratory fitness, which may provide an avenue for successful intervention.

1.1. Vascular health

As we age, large arteries become stiffer, thereby increasing pulse pressure, the amplitude of the reflected wave and the pulsatility of smaller downstream vessels (O'Rourke and Hashimoto, 2007). The ascending aorta plays a predominant role in cardiac pulsation dampening so is thought to be the first and worst affected artery in the body (Fritze et al., 2012; Redheuil et al., 2010). It may therefore be the most sensitive marker of early arterial damage in otherwise healthy adults.

Because of its high baseline blood flow, the brain is one of the only organs in the body to experience pulsatile flow. This renders the brain more sensitive to the effects of age-related large artery stiffening (Laurent and Boutouyrie, 2007; O'Rourke and Hashimoto, 2007; Sierra et al., 2004). Increased pulse-wave velocity at the level of the aorta, possibly through increases in carotid pulsatility (Mitchell et al., 2011), has been shown to be associated with cerebral damage such as decreased brain volumes (Bos et al., 2012; Mitchell et al., 2011) and increased white matter hyperintensity (WMH) volumes (Bos et al., 2012; Choi et al., 2013; Mitchell et al., 2011; Rosano et al., 2013; van Elderen et al., 2011). This damage may have functional significance, because increased central pulse-wave velocity in older adults was found to be associated with decreased cognitive performance (Bos et al., 2012; Kearney-Schwartz et al., 2009; Mitchell et al., 2011; Zhong et al., 2014).

Large artery damage, especially when it occurs in conjunction with white matter vascular lesions, is likely to be also associated with poorer cortical vascular health. Cerebrovascular reactivity (CVR) is reduced in several diseases known to include vascular damage and changes in neurovascular coupling, such as stroke, dementia, and diabetes (Girouard and Iadecola, 2006; Gorelick et al., 2011; Iadecola, 2010; van Elderen et al., 2011). Furthermore, we and others have previously shown that healthy older adults show decreased blood oxygenation level dependent (BOLD) and flow CVR to CO_2 as compared with young adults (Bailey et al., 2013; Gauthier et al., 2013; Liu et al., 2013; Lu et al., 2011). However, although there is mounting evidence that vascular health and cognitive performance are related in older adults, the strength, as well as the temporal and spatial characteristics of this vascular impairment progression, and its influence on decline in specific cognitive domains remain to be determined.

1.2. Effects of cardiorespiratory fitness

Lifestyle factors can modulate age-related vascular changes (Savela et al., 2010). A healthy diet and regular exercise are the most widely recognized means to preserve autonomy and quality of life during aging (Wallace, 2005). Physically fit older adults have been shown to have lower blood pressures and higher cerebrovascular reserve (Bailey et al., 2013; Barnes et al., 2013; Bherer et al., 2013; Brown et al., 2010). Cross-sectional studies have suggested that regular exercise may be partly protective against cognitive decline (Brown and Thore, 2011; Brown et al., 2010; Churchill et al., 2002; Etnier et al., 2006; Kramer et al., 2006; Rogers et al., 1990; Yaffe et al., 2001).

It has been hypothesized that the effects of cardiorespiratory fitness on cognition may be partly mediated through preserved vascular health, because fitness has been shown to be associated with better health both at the level of large arteries (Arena et al., 2009; Binder et al., 2006; Tarumi et al., 2013) and cerebral microvessels (Bailey et al., 2013; Barnes et al., 2013; Brown et al., 2010). However, recent work suggests that the relationship between cardiorespiratory fitness and CVR may be more complex than previously thought. Thomas et al. (2013) have shown that older master athletes have lower BOLD CVR, but preserved baseline cerebral blood flow (CBF), as compared with age-matched older sedentary controls. Part of this complexity may arise from the method used to measure CVR, because arterial spin labeling (ASL), BOLD, and ultrasound are used in different studies. BOLD and ASL provide the advantage of spatial information and ASL of physiological specificity, because it is sensitive to flow rather than an ambiguous mixture of flow, volume, and metabolism, but it suffers from a low signal to noise ratio. Here, we have chosen to measure BOLD CVR to maximize sensitivity.

We have previously shown that some vascular and metabolic brain functions are impaired in healthy older adults as compared with young adults (Gauthier et al., 2013). Here, we further characterize age-related changes in aortic pulse wave velocity (PWV), BOLD CVR, as well as cardiorespiratory fitness (VO_2 max) and executive function within a group of younger and older adults. We further document the links between these parameters within the older group. We anticipate that younger adults will show higher executive function, measured as a lower reaction time on the modified Stroop task, lower aortic stiffness, higher cardiorespiratory fitness, and higher CVR than older adults. We further expect that within the older group, better performance on an age-sensitive cognitive task in healthy older adults is associated with greater aortic elasticity, higher cardiorespiratory fitness level, and higher BOLD CVR, in line with the hypothesis that preserved executive functions are partly the result of a healthy vasculature. In subsequent portions of this article, the acronym CVR should be taken to indicate BOLD CVR unless otherwise indicated.

2. Methods

2.1. Participants

Acquisitions were conducted in a cohort of 31 young (21 males, with mean age of 24 ± 3 years) and 54 older community-dwelling healthy participants (17 males, with mean age of 63 ± 5 years) on a Siemens TIM Trio 3T MRI system (Siemens Medical Solutions, Erlangen, Germany). All participants gave informed consent, and the project was approved by the Comité mixte d'éthique de la recherche du Regroupement Neuroimagerie/Québec.

Exclusion criteria for this study included significant claustrophobia, cardiac disease, hypertension or taking blood pressure lowering medication, neurologic or psychiatric illness, cognitive impairment, regular tobacco use, high alcohol consumption (more than 2 drinks per day), thyroid disease, diabetes, asthma, and ongoing use of medications known to be vasoactive (such as statins or beta-blockers), or psychoactive. Participants were all nonsmoking and had been nonsmoking for at least 5 years. All older participants met with a geriatric physician to ensure that they did not meet any of the exclusion criteria for the study. Furthermore, all participants underwent a battery of neuropsychological tests following enrollment to ensure the absence of cognitive impairment. Table 1 shows a variety of demographic and cognitive information to characterize our cohort.