Experimental Gerontology 73 (2016) 59–64

Contents lists available at ScienceDirect

Experimental Gerontology

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

Arterial stiffness is associated with age-related differences in cerebrovascular conductance

Tussana Jaruchart [a], Nijasri C. Suwanwela [b], Hirofumi Tanaka [c], Daroonwan Suksom [a,*]

[a] Faculty of Sports Science, Chulalongkorn University, Pathumwan, Bangkok 10330, Thailand
[b] Faculty of Medicine, Chulalongkorn University, Pathumwan, Bangkok 10330, Thailand
[c] Department of Kinesiology and Health Education, University of Texas at Austin, Austin, TX 78712, USA

ARTICLE INFO

Article history:
Received 17 June 2015
Received in revised form 31 October 2015
Accepted 10 November 2015
Available online 11 November 2015

Section Editor: Christian Humpel

Keywords:
Aging
Pulse wave velocity
Transcranial Doppler
Cerebral vasomotor reactivity

ABSTRACT

To determine if arterial stiffness is associated with age-related differences in cerebrovascular conductance and reactivity, twenty-eight apparently healthy sedentary young (25 ± 1 years; n = 15) and older (67 ± 1 years; n = 13) adults were studied. Brachial-ankle pulse wave velocity (baPWV) was measured as an index of arterial stiffness. Cerebrovascular reactivity was determined by measuring changes in mean blood velocity in the middle cerebral artery under normocapnic, hypocapnic and hypercapnic conditions. Mean baPWV was greater ($p < 0.05$) in older compared with young adults. At baseline, mean cerebral blood flow velocity and cerebrovascular conductance index were lower ($p < 0.05$) in older compared with young adults under normocapnic, hypocapnic and hypercapnic conditions. There were no significant group differences in cerebrovascular reactivity when they were adjusted for stimuli (i.e., end-tidal CO_2 concentrations) in most perturbation conditions except for the normocapnia to hypercapnia condition. baPWV was negatively associated with cerebrovascular conductance index at all conditions (all $p < 0.05$). We concluded that arterial stiffness was associated with age-related differences in cerebrovascular conductance and that there were no apparent age-associated differences in cerebrovascular reactivity.

1. Introduction

Cerebral blood flow and vascular conductance are tightly regulated to deliver and distribute oxygen and nutrients to active regions of the brain. Cerebrovascular reactivity (CVR) reflects the vasodilatory capacity of the cerebral arteries. Reductions in CVR can result in a decrease in perfusion in response to global vasodilatory stimuli. Assessment of the cerebrovascular response as measured by changes in middle cerebral artery velocity to alterations in arterial carbon dioxide is a well-established method to estimate the physiological reserve of cerebral perfusion (Ainsile and Duffin, 2009). CVR has been associated with subcortical infarctions and stroke (Cupini et al., 2001) and linked with cognitive declines and is impaired in patients with dementia and Alzheimer's disease (Silvestrini et al., 2006). While it has been consistently reported that aging is associated with reduced cerebral vascular conductance (Fisher et al., 2013; Toda, 2012; Kamper et al., 2004), the effect of aging on CVR, however, remains unclear. Previous studies reported a reduced (Yamamoto et al., 1980; Reich and Rusinek, 1989) or maintained (Kastrup et al., 1998; Ito et al., 2002; Schwertfeger et al., 2006; Galvin et al., 2010) CVR to hypercapnia with aging. For CVR to hypocapnic stimuli, studies have reported unchanged (Ito et al., 2002), decreased (Yamaguchi et al., 1979; Tsuda and Hartmann, 1989; Zhu et al., 2013), and even elevated (Galvin et al., 2010) CVR with increasing age.

Advancing age is associated with alterations in structure and function of blood vessel walls, resulting in decreased vascular distensibility (Mattace-Raso et al., 2006). Microvasculature in the brain is constantly exposed to pulsatile hemodynamic strain because the brain is a high flow, low impedance organ. Stiffening of arterial walls and the resulting failure to properly buffer cardiac pulsations could lead to barotrauma, elevated cerebrovascular resistance, and reduced perfusion. Age-associated alteration in large arteries (primarily arterial stiffening) and the progressive mismatch of their "cross-talk" or impedance with small cerebral arteries may induce microvascular brain damage (Scuteri et al., 2011). Indeed cerebrovascular reactivity has been associated with increased arterial stiffness in patients with coronary heart disease (Rucka et al., 2014). Arterial stiffness is significantly and inversely associated with cerebral perfusion in deep subcortical frontal white matter of middle-age adults (Tarumi et al., 2011). However, the number of studies that address the association of arterial stiffness with CVR and/or cerebral vascular conductance is very limited. Currently, there is no existing evidence that demonstrates the association of arterial stiffness and global cerebrovascular reactivity in relation to primary aging.

* Corresponding author at: Faculty of Sports Science, Chulalongkorn University, Rama 1 Rd, Pathumwan, Bangkok, 10330, Thailand.
E-mail address: daroonwanc@hotmail.com (D. Suksom).

http://dx.doi.org/10.1016/j.exger.2015.11.006
0531-5565/

Accordingly, the primary purpose of the present study was to determine the association between arterial stiffness and middle cerebral artery vascular conductance and reactivity in apparently healthy young and older adult subjects. In order to be more comprehensive in the analyses, CVR was assessed during normocapnic, hypocapnic and hypercapnic conditions. We hypothesized that older adults would exhibit increased arterial stiffness and compromised cerebrovascular conductance and CVR compared with young adults and that arterial stiffness would be significantly associated with cerebrovascular conductance as well as CVR.

2. Methods

2.1. Subjects

A total of forty-five subjects were screened (young n = 22, older adults n = 23). Individuals with a history of diabetes, cardiovascular diseases, neurological disorders, respiratory diseases, brain disorders, and chronic smoking were excluded from the study participation. Subjects with no window at temporal bone of skull for ultrasound assessment were excluded. Fifteen young (aged 19–35 years) and thirteen older (aged 61–70 years) adults were studied. All the older subjects completed the Mini-Mental State Examination and found to be normal. All subjects gave written informed consent prior to participation in the study. The study was approved by the institutional review board at Chulalongkorn University.

2.2. Study protocol

All experiments were performed in an environmentally-controlled laboratory with an ambient temperature of 25 °C. Subjects refrained from caffeinated beverages and alcohol at least 12 h before the test. After providing written informed consent for participation, study volunteers underwent a series of measurements described below.

2.2.1. General physiological characteristics

Body composition was evaluated using body composition analyzer (Whole Body Bioelectrical Impedance Analysis, ioi 353, JAWON, Korea). Blood pressure and heart rate at rest were measured with semi-automated blood pressure device (CARESCAPE V100, GE Dinamap, USA).

2.2.2. Arterial stiffness

Brachial-ankle pulse wave velocity (baPWV) was measured using a noninvasive vascular screening device (Omron, Collin VP-1000 plus, Kyoto, Japan). Measurements were performed after at least 10 min of supine rest. Blood pressure and electrocardiogram were simultaneously measured with the vascular screening device. Waveforms were obtained from plethysmographic sensors in cuffs on both arms and ankles. Pulse wave velocity is calculated from the distance between two arterial recording sites divided by transit time. Transit time was determined from time delay between the proximal and distal foot waveforms (Sugawara et al., 2005).

2.2.3. Cerebrovascular reactivity test

Cerebral blood flow velocity (CBFV) was measured on the middle cerebral artery (MCA) by ultrasound machine (CX50, Philips, USA). MCA was insonated from the left posterior temporal window using 1.8 MHz transcranial Doppler probe. Subjects were asked to wear nose clips and breathed only through a mouthpiece, with one end open to room air and the other end connected to gas mixture line. After at least 10 min of rest in supine position, baseline recordings were taken during spontaneous breathing of room air. Heart rate and blood pressure were recorded simultaneously using semi-automated blood pressure device (CARESCAPE V100, GE Dinamap, USA). End-tidal CO_2 ($EtCO_2$), an estimate of arterial CO_2 level, was measured from expired air and analyzed by the gas analyzer (Vmax Encore 29 system, yorba Linda, CA, USA). Ventilatory expired gases were continuously measured and acquired via breath-by-breath using flow sensor. During these measurements, subjects were instructed to breathe normally and avoid body movement or Valsava maneuvers. After baseline data collection, subjects underwent 1 min of maximal voluntary hyperventilation to induce a period of hypocapnia. Heart rate and blood pressure were obtained during the first 10 s of hyperventilation while cerebral blood flow in MCA was recorded during the last 20 s of hyperventilation. Following hyperventilation, a 5-minute recovery period was provided allowing cerebral hemodynamics to restore to the baseline level. Then, subjects breathed air containing a gas mixture of 5% CO_2 and 21% O_2 balanced with nitrogen spontaneously for 3 min to induce hypercapnia. The data were recorded during the last minute of hypercapnia. Pulsatility index (PI) was calculated as the difference between systolic and diastolic flow velocity divided by mean flow velocity (Alexandrov, 2011).

Cerebrovascular reactivity was calculated as a percent change in MCA-CBFV over an absolute change in $EtCO_2$. The change in cerebrovascular reactivity was calculated from the three different ranges of end-tidal CO_2 levels; normocapnia to hypocapnia, normocapnia to hypercapnia, and hypocapnia to hypercapnia. Additionally, cerebrovascular conductance index (CVCi) was calculated in order to account for the effect of blood pressure on MCA-BFV. In an attempt to reduce variability associated with CVR measures, an average of 5–10 values were used to represent CVR responses in each subject. The equations used to estimate the cerebrovascular reactivity and cerebrovascular conductance index were shown below.

Cerebrovascular reactivity index (%/mm Hg) = %ΔMiddle cerebral artery blood flow velocity/ΔEnd tidal carbon dioxide

Cerebrovascular conductance index (cm/s ∗ mm Hg) = Middle cerebral artery blood flow velocity/Mean arterial pressure

Cerebrovascular conductance index (%/mm Hg) = %Δ middle cerebral artery vascular conductance/ΔEnd tidal carbon dioxide

2.3. Statistical analyses

All data were analyzed using SPSS statistical software (SPSS version 17.0, SPSS Inc., Chicago, IL). Prior to the parametric tests, the tests for normal distribution were performed and verified. Independent-samples *t*-tests were used to compare group differences in demographic characteristics and magnitude of changes in arterial stiffness and hemodynamic variables during normocapnia, hypocapnia, and hypercapnia. Bivariate correlation (Pearson's correlation) analyses were used to examine the relations between arterial stiffness and hemodynamic measures of middle cerebral artery during cerebrovascular reactivity test. Descriptive data are expressed as mean ± SEM. An α-level of 0.05 was considered the statistical significance.

3. Results

The general characteristics of the participants are shown in Table 1. Height was lower (all $p < 0.05$) in older compared with young adults. Systolic, mean, and diastolic blood pressure values were higher (all $p < 0.05$) in older than in young adults. Body mass was not different but BMI and % body fat were higher in older than in young adults.

As shown in Fig. 1, baPWV at baseline were greater ($p < 0.05$) in older compared with young adults. Representative data of middle cerebral artery blood flow velocity and cerebrovascular reactivity during normocapnic, hypocapnic, and hypercapnic conditions are presented in Table 2. Mean cerebral blood flow velocity and cerebrovascular conductance index were lower ($p < 0.05$) in older compared with young adults under normocapnic, hypocapnic and hypercapnic conditions. Pulsatility index was not significantly difference between older and young subjects during all conditions and was not associated with baPWV. Cerebral vasodilatory response ($\Delta CBFV/\Delta EtCO_2$) at normocapnia to hypercapnia was lower in older than in young adults.