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Cerebrovascular perfusion among older adults is moderated by strength training and gender

Xiaomeng Xu [a,b,*], Beth A. Jerskey [b,c], Denise M. Cote [c], Edward G. Walsh [d], Jason J. Hassenstab [e], Maura E. Ladino [c,f], Uraina S. Clark [b,g], Donald R. Labbe [b], John J. Gunstad [h], Athena Poppas [i], Ronald A. Cohen [b,j], Richard D. Hoge [k], Lawrence H. Sweet [b,c,l]

[a] Idaho State University, Department of Psychology, Pocatello, ID 83209, USA
[b] Alpert Medical School of Brown University, Department of Psychiatry and Human Behavior, Providence, RI 02912, USA
[c] Butler Hospital Neuroimaging Center, Providence, RI 02906, USA
[d] Brown University, Department of Neuroscience, Providence, RI 02912, USA
[e] Washington University in Saint Louis School of Medicine, Departments of Neurology and Psychology, St. Louis, MO 63110, USA
[f] Columbia University Teachers College, Department of Clinical Psychology, New York, NY 10027-6696, USA
[g] Icahn School of Medicine at Mount Sinai, Department of Neurology, New York, NY 10029, USA
[h] Kent State University, Department of Psychology, Kent, OH 44242, USA
[i] Alpert Medical School of Brown University, Department of Medicine, Providence, RI 02912, USA
[j] University of Florida, Center for Cognitive Aging and Memory, Departments of Neurology, Psychiatry and Aging, Gainesville, FL 32611, USA
[k] Université de Montréal, Departments of Neuroscience and Radiology, Centre de recherche de l'institut universitaire de gériatrie, Succ. Centre-ville, Montréal, Québec H3C 3J7, Canada
[l] University of Georgia, Department of Psychology, Athens, GA 30602-3013, USA

HIGHLIGHTS

- Cerebral perfusion is important in older adults as it is linked to cognitive declines.
- Physical activity may be associated with greater cerebral perfusion.
- MRI resting state cerebrovascular perfusion data was acquired for 59 older adults.
- Women exhibited greater cerebrovascular perfusion than men.
- Strength training was associated with great perfusion for women but not men.

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ABSTRACT

Cerebral perfusion is important in older adults as it is linked to cognitive declines. Physical activity can improve blood flow in the body but little is known about the relationship between physical activity and cerebral perfusion in older adults. In particular, no study has investigated the relation between strength training and cerebral perfusion. We examined whether different types of physical activity (assessed with the Rapid Assessment of Physical Activity questionnaire) were associated with MRI cerebrovascular perfusion in 59 older adults. There was a significant interaction between gender and strength training, such that women who engaged in strength training (weight lifting or calisthenics) at least once per week exhibited significantly greater cerebrovascular perfusion than women who did not. This interaction remained significant after controlling for other physical activity, demographics, and health variables. These findings suggest that regular strength training can be beneficial for cerebrovascular health in women.

Cerebral perfusion is especially important in older adults as the aging process leads to declines in cerebral blood flow [1,2]. This has strong functional implications for older adults as hypoperfusion is associated with cognitive impairment [3] and increased risk for developing neurological disorders, including dementia [4,5], stroke [6], and leukoaraiosis [7]. Research utilizing arterial spin labeling (ASL) has shown that reduced cerebral perfusion is associated with worse cognitive functioning in older adults [8]. Insufficient blood-flow in the brain may make it more difficult to perform well on cognitive tasks such as problem solving [9], and can also have important implications for mood and affect [10]. It is

* Corresponding author at: Idaho State University, Department of Psychology, 921 S. 8th Avenue, Stop 8112, Pocatello, ID 83209, USA. Tel.: +1 208 282 3541.
E-mail addresses: xuxiao@isu.edu, Mona.xu@gmail.com (X. Xu).

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therefore important to understand the mechanisms and moderators of cerebral blood flow in older adults.

Physical activity such as strength training has been shown to increase blood flow in the body [11], however the effect that physical activity might have on cerebral perfusion is understudied, with only one paper to date on this topic. Specifically, Rogers, Meyer, and Mortel [12] found that for retirement-aged individuals, those who engaged in regular physical activity or chose not to retire had smaller age-related declines in cerebral perfusion than those who retired and did not engage in regular physical activity. However, Rogers, Meyer, and Mortel did not assess strength training, which has been shown to increase blood flow in the body, particularly in the limbs [11,13]. The purpose of our study was to investigate the relationship between strength training and cerebral perfusion. We expected that strength training would be associated with better cerebrovascular function as assessed by cortical cerebral blood flow (CBF). Because there are typically gender differences in prevalence of engaging in physical activity [14] and because strength training can affect men and women differently [15], we also examined the role of gender in the relation between strength training and perfusion.

1. Methods

1.1. Participants

We recruited participants from advertisements in Rhode Island newspapers and through an outpatient cardiology office. Participants were fifty-nine older (M_{age} = 66.68 years ± 9.63) adults (25 men, 34 women) who were predominantly (95%) Caucasian (1 participant was Asian, 2 were African American). Participants had an average of 15.98 (±2.28) years of education (see Table 1). The study received approval from institutional Internal Review Boards and all participants completed written informed consent. Participants were paid $150 for their participation.

1.1.1. Screening

We administered comprehensive screening to ensure that participants did not have a history of moderate or severe traumatic brain injury, stroke, or any other documented neurological disease. We also administered the Mini Mental State Examination (MMSE) [16] to screen for low cognitive function and excluded potential participants who scored below the cutoff score of 25. Other exclusion criteria were a diagnosis of a current psychiatric illness, history of substance abuse with hospitalization, and contraindications for magnetic resonance imaging (MRI) such as embedded metals.

1.2. Procedures

After telephone screening, participants came in for three separate sessions.

The first session involved a battery of assessments including medical history (e.g. whether or not participants had cardiovascular disease, if they were taking cardiovascular medicines), demographics, the MMSE, and The Rapid Assessment of Physical Activity (RAPA) questionnaire [17], a well validated physical activity questionnaire that was designed for adults over 50. The RAPA consists of a series of 10 yes or no questions about various types and frequencies of physical activities including sedentary, light, moderate and vigorous aerobic activity, flexibility exercises (such as yoga and stretching), and strength training. The strength training item asked participants to report whether or not they engage in “activities to increase muscle strength, such as lifting weights or calisthenics, once a week or more”. Participants also reported on their health by answering a subset of questions from the Centers for Disease Control and Prevention’s Health-Related Quality of Life questionnaire [18]. To address potential physical limitations that could affect physical activity, participants answered yes or no to the first question in the Activity Limitations Module (“Are you limited in any way in any activities because of any impairment or health problem?”). Participants also completed the Health Days Core Module, which comprised 4 questions assessing overall mental and physical health. First, participants rated their general health on a 5 point scale (poor, fair, good, very good, excellent). Second, participants reported the number of days during the past month in which their physical health was not good. Third, participants reported the number of days during the past month that their mental health was not good. And fourth, participants reported the number of days during the past month that poor physical or mental health kept them from their usual activities.

The second session of the study involved an echocardiogram which was administered by a cardiologist (A.P.) and was evaluated to determine cardiac function (cardiac output and left ventricular ejection fraction). Participants’ weights and heights were also assessed so that we could calculate Body Mass Index (BMI) using the standard formula: (mass in kg)/(height in meters)^2. Cardiac index was also calculated by dividing cardiac output by BMI, which yielded a measure of cardiac output that controlled for body size.

The third session involved MRI, including acquisition of resting state cerebrovascular perfusion data.

1.2.1. MRI data acquisition and quantification of cerebrovascular perfusion

We used a 3 T Siemens TIM Trio scanner equipped with a 32 channel head receive array with body resonator transmit to scan participants. Foam pads were placed around the head to limit motion and foam earplugs were used to attenuate scanner noise.

After a three-axis localizer scan, a 3D T_1-MPRAGE scan with 1 mm isotropic resolution was conducted. Parameters for this scan were TR = 1900 ms, TE = 2.98 ms, TI = 900 ms, and readout flip angle = 9°. This provided a 3D T_1 image dataset for gray-white matter segmentation that was used to mask non-gray matter regions. Two three-minute resting state arterial spin labeling (ASL) scans were acquired using a PICORE-Q2TIPS technique [19]. These scans allowed acquisition of 18 contiguous axial slices. In-plane spatial resolution was 3 mm^2 with a slice thickness of 6 mm. Timing parameters were TR = 2500 ms, TI_1 = 700 ms, TI_2 = 1800 ms (inversion to start of the 64^2 echo planar image readout sequence with TE = 16 ms).

T_1 weighted anatomical volumes were segmented using FreeSurfer [20,21], generating cerebral cortical ribbon boundaries. Segmentation thresholds were set such that voxels within the cortical ribbon were selected only if they were determined by SPM to be composed of at least 80% gray matter. Cerebrovascular perfusion was then calculated by averaging perfusion values (ml of blood/100 ml of tissue/min) within the segmented T1 cortical ribbon taking into account water exchange between the vascular and interstitial compartments. Thus, perfusion (f) was calculated on a pixel basis as:

$$f = \frac{\Delta M}{2\alpha q M_0 \mathrm{TI}_1 \exp(-\mathrm{TI}_2/\mathrm{T}_{1a})}$$

where ΔM is the signal difference between corresponding pixels in labeled and control images, α is the inversion efficiency (0.95 as determined with the scanner manufacturer), q is the factor taking into account the blood/tissue water partition coefficient (0.9 ml/g) and water exchange term for gray matter (0.932 for 3 T and the above acquisition parameters) [22], M_0 is the equilibrium magnetization, $TI_{1,2}$ are the inversion times given above, and T_{1a} is the arterial blood T_1.