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

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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

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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.

Table 1
Participant characteristics.

	Total sample ($N = 59$)	Men only ($N = 25$)	Women only ($N = 34$)
Sex; female *n* (%)	34 (57.63)	0 (0)	34 (100)
Age; $M_{years} \pm SD_{years}$	66.68 ± 9.63	67.40 ± 10.22	66.15 ± 9.30
Education; $M_{years} \pm SD_{years}$	15.98 ± 2.28	16.36 ± 2.58	15.71 ± 2.02
Body Mass Index; $M \pm SD$	26.22 ± 4.65	26.73 ± 4.71	25.85 ± 4.64
CVD diagnosis; *n* (%)*	20 (33.90)	13 (52.0)	7 (20.59)
Perfusion; $M_{\text{ml of blood/100 ml of tissue/min}} \pm SD$**	45.11 ± 6.21	42.82 ± 1.12	47.13 ± 0.94
Reported strength training; *n* (%)	31 (52.54)	15 (60.0)	16 (47.06)
Reported flexibility training; *n* (%)	32 (54.24)	15 (60.0)	17 (50.0)
Aerobic activity (RAPA, range 1–7); $M \pm SD$	4.76 ± 1.93	5.24 ± 1.54	4.50 ± 1.96

* Significant gender difference, $p < .05$.
** Significant gender difference, $p < .01$.

1.3. Analyses

We calculated means and standard deviations for our variables of interest (e.g. RAPA score) and conducted a series of ANOVAs and *t*-tests to investigate group differences on cerebrovascular perfusion and other variables by CVD status, gender, and type of physical activity. We conducted General Linear Model (GLM) analyses to investigate the interaction effect of gender and the different types of physical activity on cerebrovascular perfusion. GLM analyses were conducted both with and without controlling for other potential moderating factors (e.g. demographics).

2. Results

2.1. Cardiovascular health of our sample

Of the 59 participants, 20 (13 men, 7 women) had been diagnosed with cardiovascular disease (CVD). CVD patients were relatively healthy, had cardiac function within normal limits defined as >55% (mean ejection fraction of 58.25% ± 4.94) and all were receiving treatment for CVD. Participants with and without CVD had similar left ventricular ejection fractions (58.25% ± 4.94 vs. 60.26% ± 3.43), $F(1, 57) = 3.33$, $p = 073$. There were no significant differences in cerebrovascular perfusion between participants with ($M = 46.78 \pm 1.33$) and without CVD ($M = 44.51 \pm 0.95$); $t(57) = 0.03$, $p = .978$. Therefore, we collapsed these two groups during further analyses.

2.2. Physical activity

Of the 25 men in our sample, 15 reported strength training (weight lifting or calisthenics) at least once per week and 10 did not. Out of the 34 women, 16 reported strength training at least once per week while 18 did not. Fifteen men and 17 women reported engaging in flexibility training activity (stretching or yoga) at least once per week (see Table 1).

For aerobic activity, participants were scored on a 1–7 scale on the RAPA based on their responses to questions about engaging in regular sedentary, light, moderate, and vigorous aerobic activity. A score of 1 indicated sedentary behavior, a score of 7 reflected at least 20 min of vigorous activity at least 3 days per week. For men, the mean score was 5.24 ± 1.54, while for women the mean score was 4.50 ± 1.96 (see Table 1).

There were no significant gender differences in prevalence of engaging in flexibility training, strength training, or aerobic activity nor in the frequency and intensity of aerobic activity.

2.3. Perfusion differences by gender and physical activity

Consistent with the perfusion literature, women in our study exhibited greater cortical cerebrovascular perfusion ($M = 47.13 \pm 0.94$) than men ($M = 42.82 \pm 1.12$), $t(57) = 2.83$, $p = 006$. There were no significant main effects for aerobic activity, strength training, or flexibility training.

Because there was a significant perfusion gender difference in our sample, we also investigated the interactions between gender and the different types of physical activity. There were no significant interactions involving either aerobic activity and gender or flexibility training and gender. There was, however, a significant interaction between strength training and gender, $F(1, 58) = 7.39$, $p = .009$ (see Fig. 1). Women who engaged in strength training ($n = 16$) had greater perfusion ($M = 49.96 \pm 5.12$) than women who did not ($n = 18$; $M = 44.30 \pm 5.21$), $t(32) = 3.19$, $p = .003$. This difference in perfusion was not significant for men who engaged in strength training ($n = 15$; $M = 43.97 \pm 5.98$) compared to men who did not ($n = 10$; $M = 41.67 \pm 5.85$).

Because many other factors can contribute to perfusion, we further investigated the interaction between gender and strength training by controlling for various features such as demographics. The interaction between gender and strength training remained significant even after controlling for age, education, BMI, CVD status, whether or not participants were taking cardiovascular medications, cardiac index, whether or not participants reported physical limitations, self-reported physical health (all 4 items of the Healthy Days Core Module), and participation in aerobic activity and flexibility training, $F(1, 41) = 9.46$, $p = .004$. This interaction was still significant after additionally including whole brain volume (brain volume controlling for intracranial volume) as a covariate to the GLM model above, $F(1, 40) = 9.92$, $p = .003$, indicating that perfusion differences were not due to differences in brain volume (e.g. worse perfusion due to brain atrophy).

3. Discussion

This is the first study to investigate the relationships between cerebral perfusion and strength training. Consistent with past work

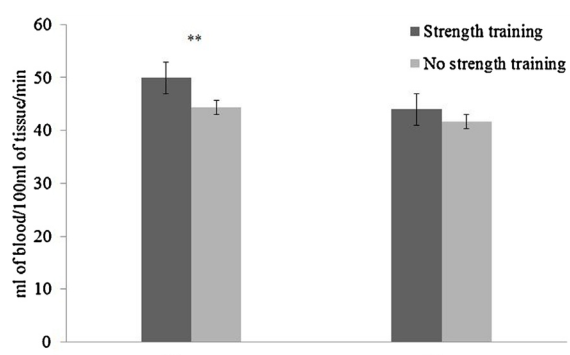

Fig. 1. Cerebrovascular perfusion as a function of gender and strength training.

with adults of all ages, including older adults [1], we found that women exhibited better cerebrovascular perfusion. We also found a significant interaction between gender and strength training such that women who strength trained at least once per week exhibited better perfusion than women who did not. This interaction was significant irrespective of other physical activity, demographic or cardiovascular measures.

Our findings are encouraging as it is important to find ways to slow down the decline of resting cerebral perfusion that occurs with normal aging. Declines in cerebral perfusion or hypoperfusion are linked to detriments in both physical and mental health including chronic fatigue [23], stroke [6], leukoaraiosis [7], depression [24], and declines in cognitive function including Alzheimer's and dementia [3–5,25–29].

Many factors may have contributed to our finding of greater resting cerebral perfusion among women who take part in resistance training. Potential mechanisms include that strength training may improve cerebrovascular function (resulting in better cerebrovascular perfusion), that those with better cerebrovascular perfusion are more likely to engage in regular strength training, or that both strength training and cerebrovascular perfusion are associated with a third variable yet to be determined (e.g. healthy choices in terms of diet and lifestyle). While our findings offer a starting point for clinical implications among older adults, future research is necessary to fully understand the mechanisms behind these results and what this means for health care providers in terms of recommendations.

The current findings are cross sectional in design and cannot be used to determine whether strength training would continue to be linked with cerebral perfusion over time, and whether or not a gender difference would persist. It is also unclear why we did not find an association between aerobic activity and cerebral perfusion, as suggested in one past study [12]. Some possible explanations include differences in our samples and measurements of physical activity. Rogers, Meyer, and Mortel focused on a global measure of activity: whether or not participants engaged in leisure time physical activities or continued to work instead of choosing to retire. We focused on physical activity in our study and did not assess for employment. It is possible that some of those who did not engage in aerobic activity in our study had also chosen not to retire, which would have offered some buffering of the decline in cerebrovascular perfusion.

One limitation of our study is the use of self-report physical activity measurements. While the RAPA was designed for assessments of older adults and has been well validated in past literature, it would be important for future studies to examine physical activity utilizing objective measures. This would be especially important in determining the mechanisms through which strength training is related to perfusion among women but not men. Some past research on strength training has shown that the muscular effects differ between men and women [15]. Future studies utilizing objective measures could also investigate the prospective effects of gender and other variables (e.g. type, duration, and intensity of physical activity) on cerebrovascular perfusion.

Overall, our findings indicate that cerebrovascular function is moderated by gender and strength training and that it may be beneficial for women to engage in strength training (such as lifting weights or calisthenics) at least once or more per week. Prospective studies are needed to investigate whether or not the link between strength training and cerebral perfusion persists over time.

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