Cerebral Blood Flow during Interval and Continuous Exercise in Young and Old Men

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Accepted for Publication: 22 January 2019
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This work was supported by a grant through the Australia-Germany Joint Research Cooperation Scheme of Universities Australia and the German Academic Exchange Service (DAAD), as well as a seed grants from the Faculty of Science, Health, Education and Engineering and the Inflammation and Healing Research Cluster at the University of the Sunshine Coast. Declaration of conflict of interest: The author(s) declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation, and the results of the present study do not constitute endorsement by ACSM.
Abstract

**Purpose:** Ageing is associated with impaired cerebral blood flow (CBF) and increased risk of cerebrovascular disease. Acute increases in CBF during exercise may initiate improvements in cerebrovascular health, but the CBF response is diminished during continuous exercise in older adults. The effect of interval exercise for promoting increases in CBF in young and old adults is unknown. **Methods:** We compared middle cerebral artery blood velocity (MCAv), end-tidal CO₂ (P_{ET}CO₂) and blood pressure (MAP) during intensity- and work-matched bouts of continuous (10-min 60%Wmax, followed by 10-min rest) and interval cycling (10x1-min 60%Wmax, separated by 1-min rest) in 11 young (25±3y) and 10 old (69±3y) men. **Results:** MCAv was higher during continuous compared with interval exercise in the young (p<0.001), but not in the old. This trend was also seen for changes in P_{ET}CO₂. While absolute MAP was higher in the old, the relative rise (%Δ) in MAP was similar between age groups and was greater during continuous exercise than interval. When we assessed the total accumulated change in MCAv (area under curve: exercise + recovery), it was higher with interval compared with continuous exercise in both groups (p=0.018). **Conclusion:** These findings suggest that interval exercise may be an effective alternative for promoting acute increases in cerebral blood flow velocity, particularly in those older adults who may have difficulty sustaining continuous exercise.

**Key words**

Ageing, cerebral perfusion, middle cerebral artery, MCAv, TCD
Introduction

Ageing and age-related neurodegenerative diseases such as dementia are associated with a reduction in cerebrovascular function and blood flow (1, 2). Habitual exercise delays the age-related reduction in cerebral blood flow (CBF) by as much as a decade in older adults, with resting CBF shown to be 17% higher in active compared with inactive older adults (1).

The primary stimulus for the beneficial effect of exercise on peripheral arterial function is thought to be attributable to the repetitive, acute increases in blood flow and shear stress on the arterial wall (3). Similar increases in CBF, measured as middle cerebral artery velocity (MCAv), are also observed during exercise and likely contribute to positive cerebrovascular adaptations (4). Identifying the type and format of exercise that induce the greatest acute increases in MCAv would help optimize exercise programs for the enhancement of cerebrovascular function (5). This is particularly important in older adults given that the acute increase in MCAv during continuous aerobic exercise is attenuated compared with younger adults (6, 7).

Interval exercise is characterized by short bouts of exercise separated by periods of rest or low-intensity recovery. This format of exercise training has become popular for promoting improvements in cardiovascular health, especially in older adults or those with chronic conditions who may have difficulty sustaining continuous exercise (8). While there is interest in the use of high-intensity interval exercise, MCAv peaks during moderate intensity exercise (~70% VO2peak) before decreasing towards baseline levels during more vigorous exercise intensities. Therefore, the use of high-intensity exercise to induce greater gains in CBF and shear stress would be counterintuitive (5). Nonetheless, the use of interval exercise at a moderate intensity may offer some advantages over traditional continuous exercise. Although MCAv increases at the onset of steady-state continuous exercise, a progressive increase in ventilation and a
downward drift in $P_{ETCO_2}$ leads to reductions in MCAv after the initiation of exercise (9). It is plausible that frequent rest periods during interval exercise would limit this reduction in $P_{ETCO_2}$, leading to a greater (10) or sustained (11) MCAv response at the same intensity of exercise. Moreover, by sustaining elevations in MCAv during short recovery periods, we hypothesized that interval exercise would lead to a greater overall accumulated cerebral flow velocity response compared with continuous exercise.

To date there have been no comparisons of the acute MCAv responses to continuous and interval exercise in younger and older healthy adults. This is important to establish the potential benefits of interval exercise on cerebrovascular health, especially in older adults who exhibit attenuated cerebral blood flow during exercise (6, 7). Therefore, the aim of this study was to compare the MCAv response between intensity- and work-matched bouts of continuous and interval cycling exercise in young and older men.

Methods

Subjects

Characteristics of eleven young (age: 25±3 years) and ten older (age: 69±3 years) male participants are summarized in Table 1. Each participant was screened prior to study entry using ACSM’s general health screening guidelines (12). Participants with hypertension (>140/90 mmHg), diabetes mellitus, hypercholesterolemia, or diagnosed cardiovascular or cerebrovascular disease were excluded from participation. None of the participants were using prescribed or over-the-counter medications or were current smokers. All experimental procedures conformed to the Declaration of Helsinki and were approved by the research ethics committee of the University of the Sunshine Coast (protocol number S16954). A detailed verbal and written
explanation of the study was provided, and prior to participation written informed consent was obtained from each participant.

**Study overview**

Participants attended the laboratory on two occasions, separated by 3-7 days. Participants attended each visit following an overnight fast, and having refrained from alcohol and physical activity for 24h, and caffeine for 12h prior. At the two experimental visits, all measurements were performed on a cycle ergometer (Corival, Lode, Groningen, Netherlands) in an upright-seated position. During the first visit, participants performed a submaximal incremental cycling exercise test. During the second visit, participants performed a bout of continuous cycling exercise at a fixed moderate intensity, and a work-matched bout of interval cycling exercise, in random order. Continuous and interval exercise bouts were separated by 30 min to allow recovery and limit any potential carryover effects (13). MCAv, MAP, $P_{ET}CO_2$ and HR were measured continuously throughout the two visits. Participants were instructed to maintain an upright posture and minimize head and eye movement during exercise to limit signal artifact. Laboratory conditions were standardized for each study visit, and external stimuli minimized. To control for diurnal variation in blood pressure and cerebral blood flow velocity, each visit for each participant was performed at the same time of day.

**Exercise protocols**

*Submaximal incremental exercise test (Visit 1).* A discontinuous, incremental protocol was used, with each exercise stage of 3 min separated by 1 min of passive recovery. The exercise workload commenced at 0 W and was increased with each stage by 25 W until a HR of 85% of the age-
predicted maximum (220-age) was reached. Pedal cadence was maintained at 60 rpm throughout the test. Based on the linear relationship between HR and workload (W), the slope method was used to determine the predicted maximum workload (Wmax) and the ACSM metabolic equation for cycling was applied to estimate the VO$_2$ at Wmax (estimated VO$_2$peak) (14).

Continuous and interval cycling exercise bouts (Visit 2). Prior to each exercise bout, participants sat quietly on the ergometer for a 5-min baseline recording. To ensure a work-matched design, both protocols included a total of 10 min of exercise. The continuous exercise consisted of 10 min of continuous cycling followed by 10 min of seated rest. This duration of exercise is consistent with the minimum periods of exercise recommended for developing and maintaining fitness in healthy adults (15). The interval exercise consisted of 10 x 1-min bouts of cycling, each separated by 1 min of seated rest. The exercise intensity of each bout was set at 60% predicted Wmax. Pedal cadence was maintained at 60 rpm throughout the continuous and interval exercise bouts.

Experimental measures
HR was monitored continuously using a 3-electrode ECG (Lead-II configuration) (ADInstrument Bio-Amp, Bella Vista, NSW, Australia). Blood pressure was measured continuously at the left middle finger using finger photophlethysmography (Finometer MIDI, Finapres Medical Systems, Amsterdam, The Netherlands) and the left forearm was supported at heart-level using a cushion, with the wrist and fingers relaxed. Participants were instructed to keep the arm and hand still throughout the cycling and recovery periods to avoid interference with the finger blood pressure signal. Finger blood pressure was exported to generate beat-by-beat continuous mean arterial
pressure (MAP = 1/3 systolic blood pressure + 2/3 diastolic blood pressure (16)) (ADInstrument, PowerLab 8/35, Bella Vista, NSW, Australia). In addition, systolic and diastolic brachial arterial blood pressure was recorded at rest and prior to each exercise bout (Carescape V100, Woodley, Bolton, United Kingdom). Rating of perceived exertion (RPE) was assessed every 2 minutes during continuous and interval exercise using the Borg RPE scale (17).

MCAv was assessed using transcranial Doppler ultrasonography (TCD, Multigon, Neurovision, Elmsford, N.Y., USA), where a 2MHz probe was placed over the temporal window. The left and right MCAv signals were identified and tested according to standardized criteria guided by signal depth, velocity and wave characteristics (18, 19). The side with the best signal quality, including the highest mean MCAv at rest, was used for testing. The ultrasound probe was fixed at a constant angle and secured with a headband (Multigon, Neurovision, Elmsford, N.Y., USA), and the signal depth, sample volume and power remained constant throughout the test session after an optimal MCAv signal was established.

Participants breathed through a leak-free respiratory mask (Hans-Rudolph, Kansas City, MO, USA), and expired air was continuously sampled (ADInstrument, PowerLab 8/35, Gas Analyzer, Bella Vista, NSW, Australia) for the determination of $P_{ET}CO_2$. MCAv, MAP, $P_{ET}CO_2$ and HR signals were sampled at 1000Hz and stored (LabChart Pro v7.3.7 and PowerLab, ADInstruments, Bella Vista, NSW, Australia). Time-aligned signals were resampled to second-by-second (1Hz) for visual inspection and analysis. Baseline data were averaged over the last minute of the resting phase prior to exercise, and minute-by-minute averages were generated for comparison between exercise conditions. To account for differences in some baseline variables
between age groups, responses during exercise were also calculated as the percent change from baseline (Δ), whilst changes in heart rate were also assessed relative to the age-predicted maximum (max). The accumulated MCAv response, including the exercise and recovery periods, was determined for each protocol by determining the area under the curve (AUC) of the absolute delta of MCAv responses from baseline.

**Data analysis**

Baseline values did not differ prior to the continuous and interval exercise tests, and we therefore averaged these data and compared between young and old groups using an independent t-test. The minute-by-minute comparison between continuous and interval cycling exercise was carried out using a three-way mixed ANOVA with the factors age (young vs. old), exercise format (continuous vs. interval) and time (min 1 to 20). The accumulated MCAv responses (AUC) to continuous and interval exercise were assessed using a two factor (age x exercise format) repeated measures ANOVA. For all ANOVA procedures, post-hoc analyses were performed using a Bonferroni correction where there were significant main effects or interactions. Pearson correlation coefficients were calculated to determine the strength of the relationships between the relative mean changes in MAP, P_{ET}CO_2, HR and MCAv during both continuous and interval exercise in young and old. All data are expressed as means ± SD, and statistical significance was set at p<0.05. Statistical analyses were performed using Statistica 7.1 (StatSoft, Tulsa, USA).

**Results**

Participant characteristics and resting cardiovascular indices are shown in Table 1. Resting diastolic blood pressure was higher, and MCAv was lower in the old, compared with the young
group. During the incremental exercise test, the young group achieved a peak workload of 243±29 W, which was higher than that achieved by the old group 145±43 W \( (p<0.001) \).

**Responses to continuous and interval exercise**

Continuous and interval exercise bouts were conducted at the same relative intensity, set at 60% \( W_{\text{max}} \). This resulted in a higher absolute workload for the young (182±25 W) compared with the older men (106±35 W, \( p<0.001 \)). Mean RPE was higher during continuous than interval exercise in both the young (Continuous: 13.3±1.3; Interval: 11.6±1.3, \( p<0.001 \)) and older men (Continuous: 14.0±1.2; Interval: 11.8±1.13, \( p<0.001 \)) and did not differ between the age groups.

The minute-by-minute responses of MCAv, MAP, \( P_{\text{ETCO}_2} \) and HR during the 20-min protocols (10 min continuous exercise, 10 min recovery vs 20 min interval) are shown in Figure 1. We observed a 3-way interaction for MCAv \( (p<0.001, \text{Figure 1}) \), where MCAv was higher during continuous exercise compared with interval exercise in the young, but not in the older men. MCAv increased during continuous exercise in both groups and was significantly elevated \( (p<0.001) \) compared to baseline from the first minute of exercise until the first minute of recovery, before returning to baseline values from the second minute of recovery. During interval exercise, MCAv increased during the first minute of exercise and remained elevated \( (p<0.001) \) compared with baseline until the 12th minute of exercise in the old group, and until the 20th minute in the young group. \( P_{\text{ETCO}_2} \), was also higher during continuous exercise in the young, but not different between exercise formats in the old. For each of these variables there were significant age effects, where absolute values for MCAv, \( P_{\text{ETCO}_2} \) and HR were higher in the young, and MAP was higher in the old. The exercise responses as \%Δ are shown in Figure 2.
The increase in %ΔMCAv during continuous exercise was greater in the young compared with the old (p<0.01, Figure 2).

Total accumulated cerebral blood flow velocity, measured as AUC of the ΔMCAv responses during the exercise and recovery periods, are shown for each exercise format in Figure 3. In line with our findings above, the AUC of ΔMCAv during exercise was greater during continuous compared with interval exercise in the young (p=0.001), but not in the old (p=0.90). AUC of ΔMCAv during the recovery periods was greater during the interval format compared with continuous in both the young and old groups (p=0.004). This resulted in a total accumulated MCAv response (exercise AUC + recovery AUC) that was higher with interval compared with continuous exercise in both the young and older men (p=0.018).

Correlations
Mean %ΔMCAv during continuous exercise was strongly correlated with the %ΔMAP (r=0.74, p<0.01) and %ΔPETCO2 (r=0.75, p<0.01) in the young group, but not in the old group (%ΔMAP, r=0.51, p=0.13; %ΔPETCO2, r=0.35, p=0.32). The mean %ΔMCAv during continuous exercise was not correlated with %ΔHR (%max) in either age group (young: r=0.16, p=0.62; old: r=0.21, p=0.55). During the 10 x 1min interval bouts, mean %ΔMCAv was strongly correlated with %ΔMAP (r=0.85, p<0.01) in the young group, but not in the old group (%ΔMAP, r=0.45, p=0.19. Mean %ΔMCAv was not significantly correlated with %ΔPETCO2 (r=0.47, p=0.14) in the young group, and moderately correlated in the old group (%ΔPETCO2, r=0.66, p=0.03).
Discussion

This study aimed to compare the effects of intensity- and work-matched interval and continuous exercise on the MCAv response in older and younger adults. We found that interval exercise induced similar increases in MCAv compared with continuous exercise in older, but not in young men. In young men the increase in MCAv was greater during continuous compared with interval exercise. When we assessed the total volume of the response (MCAv AUC) over the duration of exercise and recovery, there was a greater overall change in MCAv during interval compared with continuous exercise in both young and older men.

Consistent with most (6, 7), but not all previous reports (20), we observed a lower MCAv at rest and during exercise in older compared with young men. While interval exercise did not lead to larger increases in MCAv, we have shown that interval exercise is at least as effective as continuous exercise for increasing MCAv in older men. It has previously been suggested that interval exercise, particularly of a high-intensity, may pose a danger in older adults due to the risk that spikes in blood pressure may be transmitted to the brain (5). To the contrary, the prescribed interval exercise used in this study might offer a useful strategy to induce increases in cerebral blood flow velocity (and shear stress) without excessive rises in blood pressure. The lower perceived exertion during interval exercise in the present study suggests that this may be a more acceptable format of exercise. This is consistent with reports of greater enjoyment during high intensity interval exercise training compared with continuous exercise training in sedentary adults (21). Interval exercise may be useful exercise prescription approach for improving cerebrovascular function, particularly in older adults for whom the acute MCAv response is similar to that during continuous exercise.
In the young men, the rise in MCAv during the 1-minute exercise intervals was significantly lower than that observed during steady-state continuous exercise. At the exercise intensity used in this study (~60% Wmax), MCAv did not reach its peak until the third or fourth minute of continuous exercise, which is consistent with that reported previously (9, 22). It is likely that longer interval bouts of 4-minutes in duration would lead to a greater MCAv response in the young adults. This prescriptive approach of 4-minute exercise intervals separated by 3 min of active rest has been used in healthy and clinical groups, resulting in significant improvements in systolic blood pressure (23), cardiac autonomic and left-ventricular systolic function (24, 25) and may be superior for peripheral vascular adaptation (26, 27). Further research is needed to establish the long-term effects of interval exercise, and the optimal work:rest prescription, on cerebrovascular function in both older and younger adults.

The increase in MCAv during exercise has been shown to be largely driven by increases in \( P_aCO_2 \) and arterial blood pressure (28). In the present study, the higher overall \( P_{ET}CO_2 \) response during continuous exercise (Figure 2) might explain the higher increase in MCAv compared to interval exercise in the young. This is further supported by the strong correlation between the mean change in \( \%\Delta MCAv \) and \( \%\Delta P_{ET}CO_2 \) responses during continuous exercise in the young. It has previously been shown that only 50% of the age-associated reduction in MCAv during exercise can be attributed to the \( P_{ET}CO_2 \) response (7), and we observed no significant relationship between the change in \( \%MCAv \) and \( \%P_{ET}CO2 \) during continuous exercise in the old. The relative rise in MAP was higher during continuous compared with during interval exercise, and this corresponded with a greater rise in MCAv during continuous exercise in the young, but not in the older men. A similar dampened MCAv response, despite large increase in MAP, has
been observed in older adults previously, and might reflect an altered pressure responsiveness compared with young adults (6, 7). This is particularly evident when considering the higher absolute MAP reached during continuous compared with interval exercise in the old group in this study, as well as the strong associations between the changes in %ΔMAP and %ΔMCAv during exercise in the young, but not the older men. Further investigation is required to more fully understand the relative influence of changes in MAP and \( P_a \)CO\(_2\) on the dampened MCAv response during exercise in older adults.

Vascular adaptations with exercise training are largely attributed to the repetitive increases in blood flow and shear stress observed during acute exercise (29). Local increases in blood flow and shear stress stimulate an Akt-dependent expression of endothelial nitric oxide synthase, and the subsequent generation nitric oxide and an acute dilation response (30). With prolonged or repeated exposure to the elevations in flow and shear, structural remodeling of the vessel occurs, including an increase in vessel lumen diameter which effectively normalizes the vessel wall shear in a homeostatic fashion (29). Studies focused on the systemic (e.g. limb) vasculature have manipulated the formats and intensity of exercise to identify those that lead to the highest magnitude of these haemodynamic responses, and those that are likely to induce the greatest stimulus for adaptation (31, 32). Our study design provided the opportunity to compare not only the magnitude of the MCAv response, but also the total accumulated volume of the blood flow velocity response between exercise formats. We hypothesized that by sustaining elevations in MCAv during the short recovery periods, interval exercise may lead to a greater overall accumulated MCAv response (AUC) compared with continuous exercise. Indeed, we found a higher accumulated MCAv AUC during interval compared with continuous exercise in the old
and the young. Whether this total accumulated response (exercise+recovery) is important for future cerebrovascular adaptation is not currently known, however it would at least suggest that the acute “dose” of the blood flow and shear stress with interval exercise is greater than that achieved with continuous exercise. In a recent investigation where forearm blood flow and shear rate were manipulated using short intervals of cuff occlusion and release over a 6 week period, it was shown that the vascular adaptations, including an increase in basal blood flow, were greater than that previously reported with continuous exercise or limb heating interventions (33). The authors attributed this to the strong and persistent stimulus achieved with the interval intervention, which lends some support to potential benefits of interval exercise for promoting adaptations in cerebrovascular function and structure. Given that vascular adaptation is largely influenced by the direction of shear stress as well as the magnitude (34), determining the contribution of both antegrade and retrograde cerebral blood flow to the overall volume response, e.g. by assessing shear stress at the internal carotid artery (35), may provide further insight into the cerebral blood flow responses and the potential benefits of interval exercise for adaptation.

**Limitations**

There are some limitations of this study to consider. Exercise intensity for the interval and continuous conditions was established based on a predicted maximum workload, which was estimated with the use of an assumed age-limited maximum heart rate (i.e. 220-age). While this approach is commonly used when providing general guidance for exercise prescription, it should be noted that age-based predictions of maximum heart rate are not precise (36) and may underestimate maximum heart rate in older adults (37). As the differences in MCAv responses between age groups were very large, it is unlikely that any small error in workload estimates
between the groups would have influenced the outcomes. Furthermore, as the absolute workload was fixed across the interval and continuous exercise conditions, the use of an estimated maximum workload has no impact on our findings in relation to exercise format. Higher levels of physical activity and fitness have been associated with higher basal MCAv in some (1, 2) but not all (7) previous studies of younger and older adults. While we did not collect data on the activity status of participants, the higher estimated cardiorespiratory fitness in the young may have influenced the differences seen between age groups. Currently, TCD is the only practical measure of intracranial cerebral blood flow velocity during upright exercise. The assumption of this approach is that the cross-sectional diameter of the MCA remains constant so that increases in blood flow velocity are proportional to increases in cerebral blood flow. Although dilation of the MCA is known to occur during marked elevations (>15 mmHg) in P_{ET}CO_2 (38), in the current study the maximum changes in P_{ET}CO_2 were relatively small during the continuous (8.3±4.0 mmHg) and interval exercise (7.3±3.5 mmHg). Thus, changes in MCAv are unlikely to be influenced by changes in artery diameter during submaximal exercise, as observed previously (39). We only investigated the effect of exercise on MCAv in young and older men and therefore our findings may not be generalizable to females. Given the known influence of menstrual cycle and hormone replacement on resting MCAv (40), we specifically included males to isolate the influence of exercise format as it interacts with age. During exercise, the magnitude of the MCAv response is similar between males and females, although the kinetics of the change in MCAv are significantly slower in older females compared with older males (22). This slower MCAv response at the onset of exercise may be associated with the blunted endothelial response to exercise in post-menopausal women (41), although this remains to be determined. Moreover, because of the slowed kinetics, it is likely that MCAv would not reach its full magnitude during a
1-min bout of interval exercise in older females, which would possibly exacerbate the differences between exercise formats that we observed in older men. While it was not feasible to investigate the influence of sex in the current investigation, it is imperative that future research also includes females to address questions related to the interaction between sex and aging, especially given the greater risk of cerebrovascular disease in females with old age (42).

Conclusions
In conclusion, the acute increase in MCAv during intensity- and work-matched interval and continuous cycling exercise was not different in old men, whereas MCAv was higher during continuous exercise in young men. This suggests that interval exercise may be an effective alternative for promoting acute increases in cerebral blood flow velocity, without excessive rises in blood pressure, particularly in those older adults who may not be able to sustain continuous exercise. In both older and younger participants, the accumulated change in MCAv (AUC of MCAv during exercise and recovery) was greater with interval exercise compared with continuous exercise. Whether this reflects a greater “dose” of shear stress with interval exercise remains to be determined, and there is a now a need to investigate the cerebrovascular adaptations to interval exercise training.
Funding and acknowledgements

This work was supported by a grant through the Australia-Germany Joint Research Cooperation Scheme of Universities Australia and the German Academic Exchange Service (DAAD), as well as a seed grants from the Faculty of Science, Health, Education and Engineering and the Inflammation and Healing Research Cluster at the University of the Sunshine Coast. We thank the subjects for volunteering for this study.

Declaration of conflict of interest

The author(s) declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation, and the results of the present study do not constitute endorsement by ACSM.

Author’s contribution

TK was involved in conception and design of study, acquisition of data; analysis and interpretation of data, drafting and revising the article, final approval of the article for publication. TGB and VA were involved in interpretation of data, critical revision of article, final approval of the article for publication. SS was involved in conception and design of study, critical revision of the article, final approval of the article for publication. CDA was involved in conception and design of study, analysis and interpretation of data, drafting and revising the article, final approval of the article for publication.
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Table Legend

Table 1. Participant characteristics of resting cardiovascular indices.
Data are displayed as mean ± SD. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; Est.VO$_{2peak}$, estimated peak oxygen uptake; MCAv, middle cerebral artery flow velocity; MAP, mean arterial blood pressure; P$_{ET}CO_2$, partial pressure of end-tidal carbon dioxide; HR, heart rate.

Figure Legends

Figure 1. Absolute responses to continuous and interval exercise.
Middle cerebral artery flow velocity (MCAv; cm s$^{-1}$), mean arterial blood pressure (MAP; mmHg), end-tidal carbon dioxide (P$_{ET}CO_2$; mmHg), heart rate (HR, bpm). Data are absolute values averaged for each minute during the continuous (squares) and interval protocols (triangles) in young (Y, black filled) and old (O, open). Dotted line denotes end of the continuous exercise period. Bold numerals on the time-axis indicate the periods of exercise during the interval condition. $p$-values represent ANOVA results. Data are displayed as mean ± SD. Symbols are used to show significant exercise-format effects where: * indicates a significant difference between continuous and interval exercise in the young ($p<0.01$); † indicates a significant difference between continuous and interval exercise in the old ($p<0.01$).

Figure 2 Relative responses to continuous and interval exercise.
Middle cerebral artery flow velocity (%MCAv; % cm s$^{-1}$), mean arterial blood pressure (%MAP; %mmHg), end-tidal carbon dioxide (%P$_{ET}CO_2$; %mmHg). Data are the relative change from baseline averaged for each minute during the continuous (squares) and interval protocols
(triangles) in young (Y, black filled) and old (O, open). Dotted line denotes end of the continuous exercise period. Bold numerals on the time-axis indicate the periods of exercise during the interval condition. Heart rate is presented as the averaged responses for each minute relative to the estimated HR maximum. *p*-values represent ANOVA results. Data are displayed as mean ± SD. Symbols are used to show significant exercise-format effects where: * indicates a significant difference between continuous and interval exercise in the young (*p*<0.01); † indicates a significant difference between continuous and interval exercise in the old (*p*<0.01).

**Figure 3 Accumulated area under the curve of the MCAv responses to continuous and interval exercise**

Area under the curve (AUC) of the change in middle cerebral artery flow velocity (AMCAv) during continuous (CONT) and interval (INT) exercise in young (Y) and old (O) adults. Bars represent mean ± SD of the total AUC (exercise + recovery AUC). Filled area represents AUC of the exercise response, shaded (diagonal lines) area represents AUC of the recovery response. § Indicates a significant difference in exercise AUC compared with young interval exercise, old continuous and old interval exercise (*p*<0.01); # Indicates a significant difference in recovery AUC between continuous and interval, in young and old (*p*<0.01).
Figure 1
Figure 2
Figure 3
Table 1. Participant characteristics of resting cardiovascular indices.

<table>
<thead>
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<th>Table 1.</th>
<th>Young</th>
<th>Old</th>
<th>p-value</th>
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<tr>
<td>(n=11)</td>
<td>(n=10)</td>
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### Participant characteristics

<table>
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<th>Old (years)</th>
<th>p-value</th>
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<tr>
<td>Age</td>
<td>25±3</td>
<td>69±3</td>
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<tr>
<td>Weight, kg</td>
<td>79.3±8.3</td>
<td>77.6±9.5</td>
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<td>Height, m</td>
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<td>1.75±0.1</td>
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<td>BMI, kg m⁻²</td>
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<td>25±4</td>
<td>0.25</td>
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<tr>
<td>SBP, mmHg</td>
<td>123±10</td>
<td>128±10</td>
<td>0.28</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>65±7</td>
<td>75±6</td>
<td>0.004</td>
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<tr>
<td>Est.VO₂peak, ml min⁻¹ kg⁻¹</td>
<td>48.7±7.0</td>
<td>30.8±8.9</td>
<td>&lt;0.001</td>
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### Baseline cardiovascular indices

<table>
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<th>Young</th>
<th>Old</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCAv (cm s⁻¹)</td>
<td>67.3±8.2</td>
<td>49.9±9.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>80±12</td>
<td>95±8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PeTCO₂ (mmHg)</td>
<td>34.8±3.1</td>
<td>30.9±3.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>73±12</td>
<td>67±10</td>
<td>0.08</td>
</tr>
</tbody>
</table>
Data are displayed as mean ± SD. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; Est.\( \text{VO}_2\text{peak} \), estimated peak oxygen uptake; MCAv, middle cerebral artery flow velocity; MAP, mean arterial blood pressure; \( P_{\text{ET}}\text{CO}_2 \), partial pressure of end-tidal carbon dioxide; HR, heart rate.