Effects of High Intensity Interval Exercise on Cerebrovascular Function: A Systematic Review

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Abstract

High intensity interval exercise (HIIE) has emerged as an effective method to improve health and aerobic fitness with the benefit of decreased exercise time when compared to conventional moderate continuous exercise. However, a gap in knowledge exists regarding the effects of HIIE on contributors to overall cerebrovascular function such as cerebral blood velocity and autoregulation. The objective of this review was to ascertain the effect of HIIE on cerebrovascular function in healthy individuals. We searched PubMed and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases for articles pertaining to the apriori chosen key words. The review followed guidelines for Preferred Reporting Items for Systematic Reviews. Six articles were reviewed via the modified Sackett's quality evaluation. HIIE outcomes included middle cerebral artery blood velocity (MCAv) (n=4), dynamic cerebral autoregulation (dCA) (n=2), cerebral de/oxygenated hemoglobin (n=2), cerebrovascular conductance index (n=1), cerebrovascular resistance index (n=1), and cerebrovascular reactivity to carbon dioxide (CO₂) (n=1). Overall quality review was moderately poor ranging from 5/7 to 3/7 quality criteria met. Compared to moderate intensity exercise, HIIE resulted in a lower exercise MCAv and HIIE decreased dCA phase following exercise compared to rest. However, we report HIIE increased oxygenated and deoxygenated hemoglobin compared to rest. This systematic review outlines the cerebrovascular response during and following HIIE in healthy individuals. Future research is critically needed to better understand the effects of HIIE on cerebrovascular function in healthy individuals and individuals with chronic conditions. In order to conduct rigorous systematic reviews in the future, we recommend studies assess MCAv, dCA, and CO₂ reactivity during and post HIIE.
Introduction

High intensity interval exercise (HIIE) has emerged at the forefront of exercise regimens due to the shorter activity time needed to benefit\textsuperscript{[1-3]}. HIIE confers similar or significant increased aerobic fitness compared to conventional moderate intensity continuous exercise\textsuperscript{[1, 4-7]}. While aerobic fitness is a measure of increased cardiovascular health, the entire vascular system (including the cerebral vascular system) may be improved following increased aerobic fitness\textsuperscript{[8]}. A review and meta-analysis of HIIE in healthy adults has shown significant increases in aerobic fitness \textsuperscript{[1, 5, 6, 9]}. However, the effects of HIIE on cerebrovascular function have not been systematically reviewed.

Cerebrovascular function is the ability of the cerebral blood vessels to deliver oxygen and nutrients for neuronal metabolism and maintain cerebral blood flow through dynamic autoregulation (dCA). dCA is the ability of the brain to sustain a constant cerebral blood flow despite large fluctuations in peripheral blood pressure\textsuperscript{[10] \[11]. During resting conditions cerebral blood flow responds to arterial blood pressure fluctuations, neuronal metabolism, cortical activation, arterial blood gases, and cardiac output \textsuperscript{[12]. Cerebral blood flow can be measured at rest using magnetic resonance imaging or transcranial Doppler ultrasound (TCD). Middle cerebral artery blood velocity (MCA\textsubscript{v}) measured by TCD is the only technique to measure cerebral blood flow during exercise, with high temporal resolution \textsuperscript{[13]. MCA\textsubscript{v} is linearly related to cerebral blood flow with the caveat that the MCA diameter remains unchanged\textsuperscript{[14].}

Cerebrovascular response to submaximal exercise results in increased cerebral blood flow \textsuperscript{[15-17]}, increased cerebral oxygenation \textsuperscript{[18, 19]}, and sustained dCA\textsuperscript{[20, 21]}. MCA\textsubscript{v} has been shown to increase in parallel with exercise up to moderate intensity \textsuperscript{[15, 22-25]}. During continuous high intensity exercise and hyperventilation, MCA\textsubscript{v} is decreased due to a reduction in arterial carbon dioxide (CO\textsubscript{2})\textsuperscript{[26, 27]} causing downstream arteriole constriction\textsuperscript{[12, 28]. Cerebrovascular reactivity is
the ability of the small vessels in the brain to vasodilate and vasoconstrict in response to fluctuating CO₂ levels \cite{29, 30}.

Therefore, cerebrovascular function measures provide real-time dynamic responses within the cerebrovascular system during HIIE. Previous scientific statements and narrative reviews have recounted the latent physiological effects of HIIE on cerebrovascular function\cite{31, 32}. However, studies involving cerebrovascular function during HIIE have not been systematically reviewed. The purpose of this systematic review was to address this gap in knowledge and report the effects of HIIE on cerebrovascular function compared to moderate continuous exercise or rest conditions. We systematically examined the results of HIIE studies in healthy individuals based on the operationalization of cerebrovascular outcomes.

**Methods**

This review follows the guidelines for Preferred Reporting Items for Systematic Reviews \cite{33}. Literature searches and reviews were performed using PubMed and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases. The University of Kansas Medical Center Online Library system was used to access these databases in February - March 2020. In this systematic review, we included peer-reviewed manuscripts written in English from January 2010 to March 2020. We also incorporated inclusion of literature via recommendation emails in March 2020 from experts in the field.

Key words used to search the databases included “high intensity interval training”, “HIIT”, “high intensity interval exercise” “HIIE” AND “cerebral blood flow”, “cerebral blood velocity”, “dynamic autoregulation”. We believe these key words primarily reflect high intensity interval intervention and cerebrovascular function outcome measures. The main outcomes of this systematic review were MCAv and dCA. However, additional cerebrovascular measures were also included such
as oxygenated hemoglobin, cerebrovascular reactivity, cerebrovascular conductance index, and cerebrovascular resistance index. Cerebrovascular conductance index is a measure of the conductance of peripheral blood pressure to cerebral blood velocity and is calculated as MCAv/mean arterial pressure (MAP). Cerebrovascular resistance index (MAP/MCAv) measures the resistance of cerebral perfusion pressure to cerebral blood velocity.

The identified abstracts from PubMed and CINAHL were screened using the following inclusion criteria: 1) experimental or quasi-experimental, 2) aerobic exercise identified as the primary means of performing HIIE, 3) cerebrovascular measures were primary or secondary outcomes, and 4) human subjects across the lifespan with no current disease. After the removal of duplicates, 2 researchers screened titles/abstracts for inclusion criteria (A.W. and M.A.). The full texts were examined, and data extracted (A.W. and M.A.). If the authors were unable to come to an agreement, a third author moderated incongruity (A.F.).

A quality review was performed for each article using the modified version of Sackett’s 1981 criteria. We critically analyzed each article’s study design, population, HIIE protocols, cerebrovascular outcomes, and results. If an article did not report enough information to determine sufficient quality criteria a “No” rating was given. Articles were rated based on the level of evidence including level 1 for large randomized control trials, level II for small randomized trial, level III for nonrandomized design, Level IV for case series, and Level V for case reports.

Results

The search methods resulted in 64 articles. After removal of duplicates, 12 articles were identified in PubMed and 5 new articles in CINAHL. One recent article (published March 2020) was not recovered through key word searches. However, experts in the field
recommended the recently published article to the authors. During the initial screening of titles/abstracts, 11 articles were excluded due to HIIE not being the primary experimental protocol performed (n=6), studies not measuring cerebral arteries (n=4) and an animal study (n=1). Studies that combined other interventions with HIIE were excluded due to the confounding variables that could affect cerebrovascular outcomes. After the full text assessment, 1 article was excluded due to not meeting experimental or quasi experimental criteria (n=1). [See Figure 1 at end of document]

We included 6 articles describing cerebrovascular outcomes following HIIE within this review. The full texts are described in Table 1. [See Table 1 at end of document]. Of the articles reviewed 5 were small, randomized trials and 1 nonrandomized cross-over trial. All the studies involved healthy individuals although some only included men (n=1), women (n=1), or children (n= 1). Prior activity levels of participants ranged from inactive, recreationally active and endurance trained.

High Intensity Interval Protocols
Methods of prescribing HIIE varied greatly between studies. HIIE protocols included 6 to 16-week exercise interventions (n = 3) or 1 single bout of exercise(n=3). By examining 6 to 16 weeks of HIIE, the long-term or chronic effects of this intervention were studied. By examining a single bout of HIIE, the immediate or acute effects of the exercise were reported. In addition to the duration variability, we found that the mode of HIIE also differed across the included studies. One study used a treadmill as the mode of exercise with 4-minute intervals of 90-95% maximal heart rate for 30 minutes. The remaining 5 studies used cycling as the mode of exercise but differed in parameters ranging from 30 seconds to 7-minute intervals at 85% to 115% of maximal watts or ~ 85% to 90% maximal heart rate. A constant between all studies included an
active (rather than passive) recovery interval between sprints. However, the intensity and
duration of recovery intervals differed greatly.

Cerebrovascular Outcome Measures

The results of this review can be operationalized based on the outcome variables measured
during HIIE such as MCAv (n=4), dCA (n=2), cerebral de/oxygenated hemoglobin (n=2),
cerebrovascular reactivity to CO₂ (n=1) and cerebrovascular conductance/resistance index
(n=1). Table 3 describes whether HIIE increased, decreased or had no influence on the
operationalized cerebrovascular measures. [See Table 3 at end of document] A meta-analysis
was not performed due to low number of studies (≤2) reporting each operationalized
cerebrovascular measure.

MCAv

Of the studies reporting MCAv outcomes, resting MCAv (n = 2), exercise MCAv (n = 2) and
MCAv immediately post exercise (n = 1) were used. No significant differences were found for
resting MCAv after 6 or 12 weeks of HIIE when compared to moderate continuous exercise or
control[^37, 40]. During HIIE, exercise MCAv was significantly decreased compared to moderate
continuous exercise[^50, 53]. Conflicting results were found between two studies comparing
exercise MCAv to rest. Burma et al[^53] reported no significant difference between average
exercise MCAv and rest in adults. However, rather than reporting average exercise MCAv of the
entire HIIE bout, Tallon et al[^50] reported exercise MCAv for each 1-minute sprint interval of HIIE.
During the 6th sprint interval of HIIE, Tallon et al[^50] reported significantly decreased exercise
MCAv compared to rest which remained immediately following and up to 30 minutes post
exercise[^50].

dCA
Transfer function analysis of dCA was reported in the very low and low frequency bands (n = 2). Drapeau et al[37] conducted a 6-week intervention of HIIE and reported a significant decrease in phase compared to rest with no significant change in coherence or gain. Burma et al[53] conducted a single bout of HIIE and reported decreased MCAv systolic phase immediately following exercise that extended up to 4 hours later.

De/Oxygenated Hemoglobin

Oxygenated and deoxygenated hemoglobin were reported during a single bout of HIIE (n=1) and during a 16-week HIIE intervention (n=1). Monroe et al[51] conducted a single bout of HIIE and reported an increase in oxygenated and deoxygenated hemoglobin during HIIE compared to moderate continuous exercise. Coetsee et al[43] conducted a 16-week intervention of HIIE and reported no significant lasting changes in oxygenated or deoxygenated hemoglobin during cortical activation.

Cerebrovascular Reactivity, Conductance, and Resistance

The other outcomes measures such as cerebrovascular reactivity to CO₂, cerebrovascular conductance index, and cerebrovascular resistance index were only reported in a single study each. Cerebrovascular reactivity to CO₂ was not significantly different following 12 weeks of HIIE[40]. A 6-week HIIE intervention reported no significant changes in cerebrovascular conductance index or cerebrovascular resistance index[37].

Quality Review

The quality review of each study is presented in Table 2. [See Table 2 at end of document]. Out of 7 total quality criteria, (n=1) study met 5 criteria, (n=1) study met 4 criteria, and the remaining (n=4) studies met 3 criteria. Therefore, the overall quality criteria results were moderately poor. All studies accounted for subjects and monitored the HIIE protocol parameters. No studies
reported avoidance of contamination or co-intervention. No studies reported blinding of the outcome assessments. Only Burma et al\cite{53} and Monroe et al\cite{91} reported their reliability via coefficient of reproducibility and intraclass coefficients of their measures. And only Burma et al\cite{53} and Drapeau et al\cite{37} reported validity of their respective cerebrovascular outcomes.

Discussion

This review met the objective of reporting various HIIE effects on operationalized cerebrovascular function in healthy individuals. This review is the first to systematically report the effects HIIE on cerebrovascular function compared to moderate continuous exercise and rest.

MCAv

In these studies, 6 to 12-week HIIE interventions had no effect on resting MCAv in healthy individuals. A ceiling effect may be observed for young, healthy individuals and could explain no changes in resting MCAv\cite{16}. During a single bout of HIIE, hyperventilation and downstream arteriole vasoconstriction may explain the acute decreases in exercise MCAv compared to moderate continuous exercise\cite{12, 28, 54, 55}. Vasoconstriction may also play a protective role during HIIE due to heightened peripheral blood pressure potentially causing hyper-perfusion or damage to the blood brain barrier\cite{10, 32, 56}. During a single bout of HIIE, there is contradictory evidence comparing exercise MCAv to rest. One study reported no change in average exercise MCAv compared to resting. Another study reported decreased exercise MCAv after 6 intervals of HIIE and remained decreased compared to rest immediately following and up to 30-minutes after HIIE\cite{50}. The differences reported in exercise MCAv compared to rest could be due to age (adults versus prepubertal children) or due to the analysis of MCAv during HIIE (average over entire exercise versus separate sprint intervals). Decreases in exercise MCAv compared to rest
may only occur in the late intervals of HIIE, during hyperventilation. Therefore, exercise MCAv should be reported for each interval of HIIE rather than an average of the entire exercise bout.

dCA

After a 6-week intervention and single bout of HIIE, dCA phase was decreased compared to rest. In healthy individuals, increased frequency within MCAv and MAP waveforms (that can occur with HIIE) caused a reduction in phase due to dCA being a high-pass filter\textsuperscript{[57, 58]}. Burma et al\textsuperscript{[53]} also suggests that systolic phase may reveal greater changes than both diastolic and mean phase.

Although not included in this review due to the observational study design, contradictory evidence of sustained dCA during HIIE has been reported\textsuperscript{[41]}. Differences in exercise parameters between HIIE may be the cause to contradictory findings due to exhaustive exercise showing decreased dCA \textsuperscript{[59, 60]}. More studies are needed to confirm the acute and chronic decreases in dCA following HIIE.

De/Oxygenated Hemoglobin

After a 16-week HIIE intervention, oxygenated and deoxygenated hemoglobin during cortical activation did not change. However, the 16-week HIIE intervention decreased reaction time during cortical activation and therefore may have increased efficiency of cortical oxygen use. Also, during a single bout of HIIE oxygenated and deoxygenated hemoglobin increased compared to moderate continuous exercise. The acute and chronic effects of HIIE on oxygenated and deoxygenated hemoglobin still needs further investigation due to each only being reported in a single study.

Cerebrovascular Reactivity, Conductance, Resistance
Due to cerebrovascular reactivity, conductance index or resistance index being reported in only a single study, no conclusive effects of HIIE can be determined. However, 6 to 12 week HIIE interventions may not produce changes in cerebrovascular reactivity due to vascular desensitization from chronic exposure to CO\textsubscript{2} during HIIE\textsuperscript{[61]}.

Article Limitations
The individual study limitations have been previously acknowledged within the published articles or have been identified by authors (AW and MA) during the quality review. Most of the studies were small, randomized trials and included only healthy individuals. The small sample size available in males (n = 17), females (n = 17), or children (n = 8) limit the generalizability of results presented in this systematic review to a larger population. All studies implemented HIIE protocols that differed in time, repetitions and intensity levels, therefore making comparisons between studies difficult. These studies report potential limitations to the methods of measuring cerebrovascular function. TCD is the preeminent method of measuring MCA\textsubscript{v} during exercise but MCA\textsubscript{v} during HIIE may be underestimated\textsuperscript{[62]}. However, these studies report the minor changes in expired CO\textsubscript{2} during HIIE were not likely to induce changes in MCA diameter\textsuperscript{[14, 50, 51]}. The studies also report underestimation of cerebral oxygenation due to the two-channel near infrared spectrometer not measuring the motor, occipital, or parietal cortex \textsuperscript{[43, 51]}.

Review Limitations
The authors acknowledge a risk of publication bias by only including peer-reviewed articles written in English and did not include grey literature. The cerebrovascular function measures included within this review vary greatly and have vast heterogeneity. While HIIE is not a new mode of exercise, studying cerebrovascular measures during HIIE is novel. Therefore, authors could only identify 6 small studies with the oldest article dating back to 2015. The primary
outcome of MCAv (n=4) and dCA (n=2) were reported in few studies with low power. Therefore, a meta-analysis could not be performed due to insufficient mathematical combination.

**Conclusion**

This review has provided preliminary information studying cerebrovascular function with HIIE. We propose that a single bout of HIIE may decrease MCAv, decrease dCA, and increase oxygenated hemoglobin during or immediately following HIIE compared to moderate continuous exercise or rest conditions. However, no significant effects on resting MCAv, cerebrovascular reactivity to CO₂, cerebrovascular conductance index or cerebrovascular resistance index were found after weeks of HIIE interventions. With increased interest in healthy brain aging and implementing interventions to maintain or improve brain health, studying the effects of HIIE interventions are critically needed. While this review only included healthy individuals, we provide an early reference to understanding “normal” physiological effects of HIIE on cerebrovascular function and the need to compare to clinical populations.

Future HIIE research is needed to evaluate cerebrovascular function during and immediately following exercise. More studies such as randomized controlled trials with large sample sizes are needed to conduct a meta-analysis to combine and statistically analyze the summary results of HIIE on cerebrovascular function. Additionally, more studies are needed to determine the optimal parameters for HIIE and cerebrovascular function for humans.
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HIIE = high intensity interval exercise

Figure 1: Flow Diagram of Study Selection

Articles identified in database searches of PubMed and CINAHL (n=64)

Removal of duplicate articles identified during database searches (n=47)

Articles screened by title/abstract (n=18)

Article identified via recommendation from experts in the field (n=1)

Articles excluded (n=11)
- HIIE not primary protocol (n=6)
- Not measuring cerebral arteries (n=4)
- Animal study (n=1)

Full text articles assessed for eligibility (n=7)

Articles included in review (n=6)

Article excluded due to non-experimental or quasi-experimental study design (n=1)

Removal of duplicate articles identified during database searches (n=47)
| Study            | Design                        | Level of Evidence | Subjects       | Intervention                                                                 | Outcome measures                                                                 | Results                                                                                     |
|------------------|-------------------------------|-------------------|----------------|-----------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| Burma et al, 2020 | Small Randomized Cross-Over Trial | II                | 9 Young Adults | 3 cycling conditions:                                                       |                                                                                       | Significant increase in exercise MCAv during MICT (69 ± 5.6) compared to HIIT (58 ± 11.0, p<.05) and baseline (63 ± 7.2, p<.05). |
|                  |                               |                   |                | - High intensity interval training (HIIT, 1-min interval at 85-90% predicted heart rate reserve with 1-min active recovery 15% power output for 10 intervals) |
|                  |                               |                   |                | - Moderate intensity continuous exercise (MICT, 50-60% predicted heart rate reserve for 45 min) |
|                  |                               |                   |                | - No-exercise control                                                      | Average Exercise MCAv dCA via Transfer Function Analysis during forced MAP oscillations (repeated squat-stand maneuver) |
|                  |                               |                   |                |                                                                             |                                                                                       | No significant change in exercise MCAv during HIIT compared to baseline (p>.05).             |
|                  |                               |                   |                |                                                                             |                                                                                       | Significantly higher systolic gain/phase compared to diastolic/mean gain/phase at 0.05 and 0.10 Hz during control (p<.05). |
|                  |                               |                   |                |                                                                             |                                                                                       | Decreased systolic phase in 0.05 Hz immediately following HIIT (p>.102) and MICT until hour 4 (p>.079). |
|                  |                               |                   |                |                                                                             |                                                                                       | Decreased systolic phase in 0.10 Hz immediately following HIIT until hour 2 (p>.11) and immediately following MICT until hour 4 (p>.079). |
|                  |                               |                   |                |                                                                             |                                                                                       | No change in gain or coherence in 0.05 Hz or 0.10 Hz during HIIT or MICT. |
| Coetsee et al, 2017 | Small Randomized Controlled Trial | II | 67 Inactive Adults | 16-week intervention Treadmill 30 min, 3x/week 4 groups:  
- High intensity Interval training (HIIT, 4 min interval at 90-95% HRmax with 3 min active recovery 70% HRmax)  
- Moderate continuous training (MCT, 70-75% HRmax)  
- Resistance training (RT, 50,75,100% 10 RM)  
- No-exercise control (CON). | Cerebrovascular measures taken during cortical activation (Stroop test):  
- Oxygenated Hemoglobin  
- Deoxygenated Hemoglobin  
- Total Hemoglobin Index | No significant differences in oxygenated (effect size=.45, p=.3), deoxygenated (effect size=.67, p=.14), or total hemoglobin (effect size<.6, p>.18) after HIIT.  
Significant decrease in deoxygenated hemoglobin (effect size=1.14, p=.01) and total hemoglobin index (effect size=1.49, p<.01) after MCT.  
Significant increase in oxygenated hemoglobin in CON (effect size=.76, p=.03). |
| Drapeau et al, 2019 | Small Randomized Clinical Trial | II | 17 Endurance Trained Males | 6-week intervention. Cycled until exhaustion, 3x/week 2 groups:  
- HIIT 85 (1-7 min interval at 85% of maximal aerobic power, with active recovery of 50% of maximal aerobic power)  
- HIIT 115 (30sec – 1min interval at 115% of maximal aerobic power, with active recovery of 50% of maximal aerobic power). | Resting MCAv  
Resting CVCi  
Resting CVRi  
dCA via Transfer Function Analysis during forced MAP oscillations (repeated squat-stand maneuver) | Significant decrease in phase at 0.10 Hz in HIIT 85 and HIIT 115 (p = .048) with no differences between intensity groups.  
No significant difference in power spectral density (p > .39), gain (p > .05), or coherence (p>.05) between time or intensity.  
No significant differences in MCAv (p = .4), CVCi (p = .87), or CVRi (p = .87). |
| Study | Design | Sample | Intervention | Outcome | Findings |
|-------|--------|--------|--------------|---------|----------|
| Northey et al, 2019 | Small Randomized Controlled Trial | II 17 Female Breast Cancer Survivors | 12-week intervention Cycled 20-30 min 3x/week 3 groups:  - High intensity interval training (HIIT, 30 sec intervals at ~90% maximal heart rate or ~105% peak power with 2 min active recovery)  - Moderate intensity continuous exercise (MOD, 55-65% peak power)  - No-exercise control (CON) | Resting MCAv, Cerebrovascular Reactivity to CO₂ | No significant differences in resting MCAv (p=.24) or cerebrovascular reactivity (p=.54) after HIIT compared to MOD. No significant differences in resting MCAv (p=.86) or cerebrovascular reactivity (p=.72) after HIIT compared to CON. |
| Tallon et al, 2019 | Small Randomized Cross-over Trial | II 8 Prepubertal Children | 2 Cycling conditions:  - High intensity interval exercise (HIIE, 1 min interval at 90%max watt with 1 min active recovery at 20%max watt for 6 intervals)  - Moderate-intensity steady-state exercise (MISS, 15 min at 44%max watt) | Exercise MCAv during each interval  Immediate post-exercise MCAv  30-minutes post-exercise MCAv | Significant decrease in exercise MCAv during the 6<sup>th</sup> interval of HIIE compared to baseline (10.7%, p=.004). Significant decrease in exercise MCAv during the 3<sup>rd</sup> and 4<sup>th</sup> intervals of HIIE compared to MISS (p=.001). Significant decrease in MCAv immediately post-exercise following HIIE and MISS (p<.001). No significant difference in MCAv at 30-minutes post-exercise following HIIE and MISS compared to baseline (p>.05). Significant increase in exercise MCAv during the 2<sup>nd</sup> minute of MISS compared to baseline (5.8%, p=.004). |
| Monroe et al, 2015 | Nonrandomized Cross-Over Trial | III | 15 Recreationally Active Adults | 2 cycling conditions:  
- Sprint Interval Cycling (SIC, 30 second all-out sprint interval with 4 min active recovery for 4 intervals)  
- Constant Resistance Cycling (CRC, 18 min at 70rpm with resistance set by matching total work performed during SIC) | Oxygenated Hemoglobin (HbO2)  
Deoxygenated Hemoglobin (HHb) | Significant increase in average HbO2 (effect size=.536, p=.001), minimum HbO2 during recovery (effect size=.392, p<.001), and maximum HbO2 during recovery (effect size=.588, p=.001) in SIC compared to CRC.  
Significant increase in average HHb during SIC compared to CRC (effect size=.386, p=.003).  
Significant increase in average HbO2 (effect size=.373, p=.001), minimum HbO2 during recovery (effect size=.223, p=.038), and maximum HbO2 during recovery (effect size=.333, p=.006) in men compared to women.  
Significant increase in average HHb (effect size=.198, p=.034), minimum HHb during recovery (effect size=.264, p=.012), and maximum HHb during recovery (effect size=.358, p=.001) in men compared to women. |

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MCAv = middle cerebral artery blood velocity, dCA = dynamic cerebral autoregulation, min = minute, HRmax = maximum heart rate, CVCI = cerebrovascular conductance index, CVRI = cerebrovascular resistance index, CO₂ = carbon dioxide
Table 2: Summary of Quality Review

| Study                          | Avoided Contamination and Co-Intervention | Random Assignment to Conditions | Blinded Assessment | Monitored Intervention | Accounted for All Subjects | Reported Reliability of Measures Used | Reported Validity of Measures Used | Total Number of Criteria Met |
|-------------------------------|------------------------------------------|-------------------------------|-------------------|------------------------|---------------------------|--------------------------------------|----------------------------------|-----------------------------|
| Burma et al, 2020             | No                                       | Yes                           | No                | Yes                    | Yes                       | Yes                                  | Yes                              | 5                           |
| Coetsee et al, 2017          | No                                       | Yes                           | No                | Yes                    | Yes                       | No                                  | No                               | 3                           |
| Drapeau et al, 2019          | No                                       | Yes                           | No                | Yes                    | Yes                       | No                                  | Yes                              | 4                           |
| Northey et al, 2019          | No                                       | Yes                           | No                | Yes                    | Yes                       | No                                  | No                               | 3                           |
| Tallon et al, 2019           | No                                       | Yes                           | No                | Yes                    | Yes                       | No                                  | No                               | 3                           |
| Monroe et al, 2015           | No                                       | No                            | No                | Yes                    | Yes                       | Yes                                 | No                               | 3                           |
| Study                        | Resting MCAv | Exercise MCAv | Post-Exercise MCAv | dCA phase | dCA Gain | dCA Coherence | De/Oxy-genated Hemoglobin during Cognition | De/Oxy-genated Hemoglobin during Exercise | Resting Cerebrovascular Conductance/Resistance Index | Cerebrovascular Reactivity to CO₂ |
|------------------------------|--------------|---------------|--------------------|-----------|----------|---------------|--------------------------------------------|-------------------------------------------|--------------------------------------------------------------------------------|----------------------|
| Burma et al, 2020            |              |               |                    | ↓         |          |               |                                            |                                           |                                                                               |                      |
| Coetsee et al, 2017          |              |               |                    |           |          |               |                                            |                                           |                                                                               |                      |
| Drapeau et al, 2019          | ○            |               |                    |           |          |               |                                            | ○                                         |                                                                               |                      |
| Northey et al, 2019          | ○            |               |                    |           |          |               |                                            |                                           |                                                                               |                      |
| Tallon et al, 2019           |              |               |                    | ↓ to moderate and rest | |     |               |                                            |                                           |                                                                               |                      |
| Monroe et al, 2015           |              |               |                    |           |          |               |                                            |                                           |                                                                               |                      |

\(\downarrow\) = Decreased effect, \(\uparrow\) = Increased effect, \(\bigcirc\) = no effect