Passive Exercise Increases Cerebral Blood Flow Velocity and Supports a Postexercise Executive Function Benefit

Mustafa Shirzad[a], Benjamin Tari[a], Connor Dalton[a], James Van Riesen[c], Michael Marsala[a], Matthew Heath[a, b, c]

[a]School of Kinesiology, Faculty of Health Sciences, University of Western Ontario, 1151 Richmond St, London, ON N6A 3K7, Canada
[b]Canadian Centre for Activity and Aging, University of Western Ontario, 1201 Western Rd, London, ON N6G 1H1, Canada
[c]Graduate Program in Neuroscience, University of Western Ontario, 1151 Richmond St, London, ON N6A 3K7, Canada

Running Head: Passive exercise and executive function

Correspondence to:
Matthew Heath
School of Kinesiology
The University of Western Ontario
London, Ontario, Canada
N6A 3K7
Email: mheath2@uwo.ca
Phone: 519-661-2111 ext# 80498

-June 9, 2022, v. 3.0-

Abstract

Executive function entails high-level cognitive control supporting activities of daily living. Literature has shown that a single-bout of exercise involving volitional muscle activation (i.e., active exercise) improves executive function and that an increase in cerebral blood flow (CBF) may contribute to this benefit. It is, however, unknown whether non-volitional exercise (i.e., passive exercise) wherein an individual's limbs are moved via an external force elicits a similar executive function benefit. This is a salient question given that proprioceptive and feedforward drive from passive exercise increases CBF independent of the metabolic demands of active exercise. Here, in a procedural validation participants (n=2) used a cycle ergometer to complete separate 20-min active and passive (via mechanically driven flywheel) exercise conditions and a non-exercise control condition. Electromyography showed that passive exercise did not increase agonist muscle activation or increase ventilation or gas exchange variables (i.e., $\dot{V}O_2$ and $\dot{V}CO_2$). In a main experiment participants (n=22) completed the same exercise and control conditions and transcranial Doppler ultrasound showed that active *and* passive exercise (but not the control condition) increased CBF through the middle cerebral artery (ps<0.001); albeit the magnitude was less during passive exercise. Notably, antisaccade reaction times prior to, and immediately after, each condition showed that active (p<0.001) *and* passive (p=0.034) exercise improved an oculomotor-based measure of executive function, whereas no benefit was observed in the control condition (p=0.85). Accordingly, results evince that passive exercise 'boosts' an oculomotor-based measure of executive function and supports convergent evidence that increased CBF mediates this benefit.

Keywords: *antisaccade; cognition; cortical hemodynamics; oculomotor; transcranial Doppler ultrasound;*

1. Introduction

Executive function entails the high-level cognitive control components of inhibitory control, working memory, and cognitive flexibility – components essential to successful activities of daily living (Diamond, 2013; Miyake et al., 2000). Accumulating literature has demonstrated that a single bout of aerobic and/or resistance exercise across a continuum of intensities provides a transient improvement (i.e., <60-min) to executive function (Barella et al., 2010; Hung et al., 2013; Shukla & Heath, 2020; for meta-analyses see, Chang et al., 2012; Lambourne & Tomporowski, 2010; Ludygda et al., 2016). A candidate mechanism contributing to this improvement is an exercise-mediated increase in cerebral blood flow (CBF). Indeed, exercise initiates a rapid rise in CBF via CO_2 production from volitional muscle activation, increased diffusible molecules (e.g., nitric oxide: NO), heart rate, ventilation, and concomitant vascular deformation increasing systolic blood pressure (Smith & Ainslie, 2017). The increase in CBF has been linked to temperature- and mechanical-based changes to the brain's neural and glial networks that enhance the efficiency of local neural circuits involved in information processing (i.e., the hemo-neural hypothesis; see Moore & Cao, 2008). As well, chronic hypoperfusion linked to age- and disease-related states impairs executive function (Bertsch et al., 2009). Accordingly, the combined exercise and hypoperfusion literature evince a bi-directional relationship between CBF and executive function.

In further support for the role of CBF in a postexercise executive function benefit, our group had participants complete a 10-min single bout of aerobic exercise via cycle ergometer, and a condition wherein participants inhaled a higher-than-atmospheric concentration of CO_2 for 10-min without exercising (i.e., hypercapnia) (Tari et al., 2020). The hypercapnic environment was used because it produces a rapid increase in CBF independent of the metabolic demands of

exercise (Kety & Schmidt, 1948; Raper et al., 1971; Ito et al., 2000). Notably, Tari et al. had participants perform the hypercapnic condition first so that changes in CBF across conditions could be matched via real-time transcranial Doppler ultrasound (TCD) monitoring of blood flow velocity (BV) through the middle cerebral artery (MCA). Tari et al. employed a pre- and post-condition assessment of executive function via an oculomotor task (see details below) and results showed that exercise and hypercapnia conditions produced reliable – and equivalent magnitude – improvements in the oculomotor-based index of executive function, whereas a non-exercise, non-hypercapnic control condition did not elicit a pre- to post-condition change in the same index of executive function. Based on these results, Tari et al. proposed that an increase in CBF supports a postexercise improvement in executive function.

Although ample evidence indicates that aerobic and resistance exercise (so-called active exercise) increases CBF and leads to a postexercise improvement in executive function, to our knowledge no work has examined whether passive exercise similarly benefits executive function. Passive exercise occurs when a limb or joint is manipulated/moved without volitional control and is an established rehabilitation technique frequently used to improve local blood flow following an acute musculoskeletal injury, and to support long-term rehabilitation in populations with reduced (e.g., hemiparesis following stroke) or absent (e.g., spinal cord injury) mobility (for review see Trinity & Richardson, 2019). In spite of the fact that passive exercise does not generally entail any volitional muscle activation (cf. Bell & Duffin, 2003), it does induce hyperemia and increases CBF in healthy individuals (Doering et al., 1998; Matteis et al., 2003; Nagaya et al., 2015). For example, passive cycle ergometry of the lower limbs increases CBF from baseline in concert with increased cardiac output, stroke volume and systolic blood pressure (Nobrega et al., 1994; Doherty et al., 2018). As well, some work has shown that passive exercise

does not alter heart rate or respiration and occurs independent of a change in diffusible CO_2 and NO (Asahara & Matsukawa, 2018). Thus, the mechanisms associated with a passive-exercise increase in CBF are different from those associated with active exercise. The passive exercise increase in CBF has been linked to the activation of (1) mechanosensitive Group III muscle afferents that stimulate the primary somatosensory cortex and increase cardiac output and stroke volume (Nobrega & Araujo, 1993; Nurhayati & Boutcher, 1998; Gladwell & Coote, 2002) and (2) feedforward command mechanisms that alter cardiovascular centers via descending central neural pathways involved in somato-motor activity (Krogh & Lindhard 1913; Goodwin et al. 1972; Eldridge et al. 1985; Victor et al. 1995; Matsukawa, 2012).

The goals of the current study were to examine whether a passive exercise-mediated increase in CBF is associated with a postexercise improvement in an oculomotor-based index of executive function, and to contrast whether a putative improvement is equivalent to that observed following active exercise. To that end, separate passive exercise, active exercise and control conditions were included here. In the active exercise condition, participants pedalled a cycle ergometer for 20-min at a light-intensity, whereas in the passive exercise condition the same duration of exercise was implemented, and the cycle ergometer flywheel was mechanically driven with revolutions per minute (rpm) matched to the active exercise condition. In the control condition, participants sat on the cycle ergometer without passive or active exercise. In a pre-investigation procedural validation, electromyography (EMG), respiratory ($\dot{V}_E$ as well as heart rate and blood pressure) and gas exchange (i.e., $\dot{V}O_2$, $\dot{V}CO_2$,) variables were measured across each condition to ensure that our passive exercise condition did not produce volitional activation of agonist muscles and/or a task-based increase in metabolic demands. This was deemed necessary given work by Duffin and colleagues (Bell & Duffin, 2003, Bell & Duffin, 2004; Bell

et al., 2003) reporting that passive cycle ergometry (via tandem bicycle) can increase ventilation and produce a steady-state hyperpnea with continued exercise – a response that would alter blood pH and decrease CBF without a concomitant change in blood pressure. That Duffin and colleagues observed an increase in respiration during passive exercise may relate to the mode of delivery (i.e., tandem ergometer vs. mechanically driven flywheel) and/or the pedal frequency used in their work. In particular, Duffin and colleagues had participants 'passively' cycle on a tandem ergometer (i.e., the experimenter pedalled) without a feedforward cue related to pedal frequency (i.e., metronome) – a passive exercise mode requiring activation of lower leg musculature that can increase respiration. In contrast, externally timed and mechanically driven passive leg extensions did not influence respiration (see Bell & Duffin, 2006). Accordingly, we sought to verify that the passive cycle ergometry (via mechanical flywheel and a metronome-paced frequency) used here did not alter respiratory, gas exchange or cardiorespiratory measures. Subsequently, in the main experiment, TCD was used to estimate BV through the MCA in each condition. As in previous work by our group (Dirk et al., 2020; Heath et al., 2019; Petrella et al., 2020; Samani & Heath, 2018; Shukla & Heath, 2021) an antisaccade task completed pre- and post-condition was used to provide an oculomotor-based index of executive function. Antisaccades require a goal-directed eye movement (i.e., a saccade) mirror-symmetrical to an exogenously presented target and produce longer reaction times (RT) (Hallett, 1978; Fischer & Weber, 1992) and less accurate and more variable endpoints than their prosaccade (i.e., saccade to veridical target) counterparts (Dafoe et al., 2007; Gillen & Heath, 2014). Extensive evidence has shown that the behavioural 'costs' of antisaccades are attributed to the two-component executive function demands of response inhibition and vector inversion (i.e., 180° spatial transformation of a target location and a feature of cognitive flexibility) (for review see, Munoz

& Everling, 2004). Moreover, human functional neuroimaging and lesion studies, and non-human primate work involving cryogenic deactivation of the prefrontal cortex, has shown that a directionally correct antisaccade is supported by a task-set that flexibly maintains behavioural rules on a moment-to-moment basis (for review see Everling & Johnston, 2013). Hence, antisaccades require top-down control supported via each core component of executive function. What is more, the frontoparietal networks supporting antisaccades are the same as those showing task-based changes in activity following single and chronic bouts of exercise (Colcombe et al., 2004; Voss et al., 2010; Verburgh et al., 2014). As such, antisaccades provide a framework for examining subtle exercise-mediated changes in executive function. In terms of research predictions, if an increase in CBF is related to an improvement in an oculomotor-based index of executive function then antisaccade RTs should decrease from pre- to post-condition assessments in passive and active exercise conditions. In contrast, if an increase in CBF is an epiphenomenon associated with passive and active exercise then the post-condition improvement in antisaccade RTs should be selectively restricted to the active exercise condition.

2. Methods

2.1. Participants

In the pre-investigation procedural validation, two participants (one female and one male aged 22 and 21, respectively) were recruited. In the main experiment, 28 participants were recruited (11 female, age range: 19–26 years) with sample size determined *a priori* via an effect size derived from previous work examining pre- to postexercise changes in antisaccade RTs (α=0.05, power = 0.99, d_z= 1.30) (Tari et al., 2020). All participants were naïve to the purpose of this study and were recruited from the University of Western Ontario community. Participants were self-reported right-hand dominant (i.e., "what hand do you write with?"), with normal or corrected-to-normal vision, no history of smoking and/or cardiorespiratory, metabolic, musculoskeletal, neurologic (including concussion), or neuropsychiatric disorder. Participants reported that they did not take medication that may affect metabolic, cardiac, respiratory, or hemodynamic responses to exercise. It was requested that participants not consume alcohol or caffeine 12 hours prior to the study and that they get 8 hours of sleep on the night prior to each data collection session. The order in which conditions were performed (in both the procedural validation and main experiment) were randomized with each completed on a different day separated by at least 24 hours. All data collection took place between 9:30 am and 12:00 pm with participants in a hydrated state (i.e., 555 ml consumed 1-hour in advance of data collection). Prior to data collection, participants read a letter of information approved by the Health Sciences Research Ethics Board, University of Western Ontario and provided informed written consent. This study was conducted according to the most recent iteration of the Declaration of Helsinki with the exception that participants were not registered in a database.

All participants obtained a full score on the 2020 Physical Activity Readiness Questionnaire (PAR-Q+) and completed the Godin Leisure-Time Exercise Questionnaire (GLTEQ). For the pre-investigation procedural validation, GLETQ scores for the female and male participant were 70 and 84, respectively. In the main experiment, the average GLETQ score was 62 (SD = 26; range: 36-96) – results indicating that all participants were recreationally active.

2.2. Apparatus and Procedure

The pre-investigation validation procedure and main experiment involved three conditions: active exercise, passive exercise and a control condition. For all conditions, participants sat upright on an active-passive cycle ergometer (E-PAT AP; Healthcare International, Langley, WA, USA) equipped with a mechanically driven flywheel and their feet secured to the ergometer pedals via Velcro straps. Participants were positioned such that their legs achieved approximately 85% of full extension at the end of an active pedal stroke. All conditions were preceded by a 2-min baselining in which participants remained stationary on the ergometer. In the active exercise condition, a 2-min warm-up followed baselining and required active cycling against a resistance of 15 W at a cadence of 40 rpm. Subsequently, a step-transition to active cycling against a resistance of 37 W (cadence = 70 rpm) was completed for a 20-min interval, after which a 2-min cool-down was performed as per the warm-up. The active exercise condition corresponds to a "light" intensity in the exercise work-rate continuum (Takata et al., 1990; Shim et al., 2013; Tari et al., 2021a). The passive exercise condition employed the same timeline as the active exercise condition (i.e., baseline, warm-up, intervention, cool-down); however, pedal cadence during warm-up, intervention and cool-down was mechanically driven and participants were instructed to not actively engage their leg muscles. During the warm-

up/cool-down, cadence was set at 40 rpm and transitioned to 70 rpm during the 20-min intervention. For the control condition, participants sat on the cycle ergometer for the baseline procedure and an additional 24-min (i.e., 26-min total: a period equivalent to warm-up, intervention, and cool-down in the exercise conditions) and watched a television sitcom on a popular streaming application. For all conditions, a metronome (MA-2-BKRD; Korg, Tokyo, Japan) was played. The metronome was used to support equivalent pedal cadence in the active and passive conditions.

2.3. Pre-investigation procedural validation

For the procedural validation, EMG from primary agonists involved in cycling were collected (Hug & Dorel, 2009) as were ventilatory, gas exchange and cardiovascular (i.e., heart rate and blood pressure) variables. Given the objective of this validation, we did not include pre- and post-condition measures of executive function.

EMG data collection. Surface EMG were recorded from 10 mm Ag/AgCL electrodes (Trigno Avanti Sensor; Delsys, Inc. Natick, MA, USA) placed on the right vastus lateralis (i.e., 2/3 distance between anterior iliac spine and the lateral side of the patella), right biceps femoris (i.e., 1/2 distance between participants' ischial tuberosity and lateral epicondyle of the tibia), and right lumbar erector spinae (i.e., ~2.5 cm laterally from the spine and in line with the iliac crest). A reference electrode was placed on the superior iliac crest. Electrode sites were cleaned with an alcohol swab, lightly abraded and coated with EMG gel (Nu-prep, Weaver and Company, CO, USA). EMG signals were amplified, bandpass filtered (i.e., 20-450 Hz) and collected (EMGworks; Delsys, Inc. Natick, MA, USA) at 1926 Hz for the vastus lateralis and biceps femoris, and at 1260 Hz for the lumbar erector spinae. MATLAB (2018b: Mathworks, Natick, Mass., USA) was used to identify windows for inspection and visually compare conditions.

Ventilatory and gas exchange data collection. Participants were fitted with a face mask (7450 Series V2 Oro-Nasal Reusable Face Mask; Hans Rudolph, Shawnee, KS, USA) providing an airtight seal around the mouth and nose to assess breath-by-breath gas exchange of O_2 uptake ($\dot{V}O2$) and CO_2 output ($\dot{V}CO_2$) via mass spectrometry (CPET; Cosmed, Rome, Italy). To provide a profile of each breath, a peak-detection algorithm was used to determine end-tidal CO_2 ($P_{ET}CO_2$) and O_2 ($P_{ET}O_2$) pressures with inspired and expired gas volumes and durations time-aligned at a sampling rate of 100 Hz. Heart rate was measured continuously by a heart rate monitor (Polar Electro T34, Kempele, Findland) using PowerLab (ML132/ML880, ADInstruments, Colorado Springs, CO, USA) and was calculated (using a 5 s rolling average) based on successive heart beats (i.e., RR interval), and blood pressure was taken at regular intervals (i.e., 3, 6, 9, 12, 15, 18, 21 and 24 min) via a manual sphygmomanometer and stethoscope (Welch Allyn FlexiPort reusable blood pressure cuff; Welch Allyn Inc. Skaneateles Falls, NY, USA) secured to participants' left upper arm.. All data post-processing matches that outlined in previous work by our group (Heath et al., 2018; Petrella et al., 2019; Dirk et al., 2020; Tari et al., 2020, 2021a).

EMG data for the female participant are presented in **Figure 1** across ten successive pedal revolutions at the 10-min mark in the active and passive conditions and an equivalent time period in the control condition. The active exercise condition shows periodized activation of the vastus lateralis – a result consistent with a wealth of evidence demonstrating muscle activation patterns for active cycling (for extensive review, see Hug & Dorel, 2009). In contrast, the passive exercise condition shows no discernable change in muscle activation and mirrors that associated with the control condition.

The ventilatory and gas exchange variables for the female participant are shown in **Figure 2**. The active condition showed increased $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$ from baseline to warm-up and a further increase during the 20-min intervention. Moreover, the baseline-to-intervention increases in $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$ are directly in line with the "light-intensity" protocol employed by Tari et al. (2021a) which required 10-min of cycling on an upright ergometer at 25 W (75 rpm). In contrast, the passive exercise condition did not show a substantial change in any variable across baseline, warm-up and intervention and corresponds to the control condition. **Table 1** shows that active condition heart rate and systolic blood pressure increased from baseline, warm-up and intervention, whereas passive exercise and control condition values did not demonstrate an appreciable change across each assessment period. EMG, ventilatory and gas exchange data for the male participant were comparable to the female participant. Thus, the procedural validation demonstrates that the passive exercise condition did not lead to activation of agonist musculature and did not render increased task-based cardiovascular or ventilatory demands.

2.4. Main experiment

The conditions used in the main experiment (i.e., active exercise, passive exercise and control) matched the procedural validation with the exceptions that neither EMG nor ventilatory data were captured. Instead, the main investigation provided an estimate of CBF via TCD through the MCA and included a pre- and post-condition examination of executive function. In addition, for the main experiment heart rate and blood pressure were taken at regular intervals (i.e., heart rate: 2, 12, 22 min; blood pressure: 12 min).

TCD data collection. For each condition, a TCD probe (Neurovision 500M, Neurovision TOC2M; Multigon Industries, Elmsford, CA) was coated in an aqueous ultrasound gel

(Aquasonic Clear, Parker Laboratories Inc., Fairfield, NJ) and secured via headband to participants' left anterior temporal window to measure blood flow velocity (BV) through the MCA. Importantly, TCD is a valid proxy for a direct measure of changes in CBF (Bishop et al., 1986).

Executive function assessment. To provide an index of executive function, an oculomotor task (with which participants were not familiarized) was completed prior to and immediately following each condition. For each assessment, participants sat on a height-adjustable chair in front of a table on which an LCD monitor (60 Hz, 8-ms response rate, 1280 × 960 pixels; Dell 3007WFP, Round Rock, TX) was located 550 mm from the table's front edge. Participants placed their head in a head-chin rest, and the gaze location of their left eye was tracked via a video-based eye tracking system (EyeLink 1000 Plus; SR Research, Ottawa, ON, Canada) sampling at 1000 Hz. Prior to data collection, a nine-point calibration and validation of the viewing space was completed (i.e., <1° of error). All experimental events were controlled via MATLAB (R2018a; The MathWorks, Natick, MA, USA) and the Psychophysics Toolbox extension (v. 3.0) (Brainard, 1997; Kleiner et al., 2007) including the EyeLink Toolbox (Cornelissen et al., 2002). The lights in the experimental suite were extinguished during data collection.

Visual stimuli were presented on a black screen (0.1 cd/m^2) and included a midline-located red fixation cross (1°: 50 cd/m^2) presented at participants' eye level and targets (i.e., open white circle; 2.5° in diameter: 127 cd/m^2) presented 15° (i.e., proximal target) and 20° (i.e., distal target) to the left and right of fixation and in the same horizontal plane. Fixation onset signaled participants to direct their gaze to its location. Once a stable gaze was achieved (i.e., ± 1.5° for 450 ms), a uniformly distributed randomized foreperiod (1000 – 2000 ms) was introduced after

which the fixation disappeared and a target appeared 200 ms thereafter (i.e., gap paradigm). Target onset cued participants to saccade mirror-symmetrical to the target location (i.e., antisaccade) as "quickly and accurately as possible". For each oculomotor assessment, 20 trials to each target location (i.e., left, and right visual field) and eccentricity (i.e., proximal, and distal) were randomly presented (i.e., 80 total trials).

2.5. Data reduction

TCD data corrupted by signal aliasing and/or signal loss (e.g., a sudden head shift) were omitted (Terslev et al., 2017) and systolic BVs were retained for analysis (Clyde et al., 1996). Systolic BVs were analyzed given Rosengarten and Kaps' (2002) demonstration that they provide a valid measure for TCD-based changes in BV through the MCA and provide a measure for increased task-based demands in oculomotor control (Duschek et al., 2018; Tari et al., 2021b). Mean values were determined via the last minute of rest (i.e., baseline) and the last minute of each intervention (i.e., steady-state).

Gaze position data were filtered offline using a dual-pass Butterworth filter with a low-pass cut-off frequency of 15 Hz. A five-point central-finite difference algorithm was used to compute instantaneous velocities and acceleration. Saccade onset was determined when velocity and acceleration exceeded 30°/s and 8,000°/s^2, respectively. Saccade offset was determined when velocity fell below 30°/s for 40 ms. Trials involving a signal loss (e.g., an eye blink) were removed as were anticipatory responses (RTs <50 ms) (Wenban-Smith & Findlay, 1991) and RTs >2.5 standard deviations from a participant- and task-specific mean (Gillen & Heath, 2014b). Less than 4% of trials for any participant were omitted. Trials involving a directional error (i.e., a prosaccade instead of an instructed antisaccade) were excluded from subsequent analyses because they are associated with planning mechanisms distinct from their directionally

correct counterparts (DeSimone et al., 2014) and accounted for less than 5% of trials. This low error rate is attributed to the fact that antisaccades were not interleaved with prosaccades.

2.6. *Dependent variables and statistical analyses*

BV data were analyzed via 3 (condition: active exercise, passive exercise, control) by 2 (time: baseline, steady-state) fully repeated measures ANOVA ($\alpha = 0.05$). Heart rate was analyzed via 3 (condition: active exercise, passive exercise, control) by 3 (time: 2-min, 12-min, 22-min) fully repeated measures ANOVA ($\alpha = 0.05$), and systolic, and diastolic blood pressure captured at the 12-min interval of each condition were assessed via separate one-way (condition: active exercise, passive exercise, control) ANOVA ($\alpha = 0.05$). Oculomotor dependent variables included RT (i.e., time from response cueing to saccade onset), interquartile range of RT (i.e., IQR of RT), saccade duration (i.e., time from saccade onset to saccade offset) and saccade gain (i.e., saccade amplitude/veridical target location). Oculomotor dependent variables were examined via 3 (condition: active exercise, passive exercise, control) by 2 (time: pre-, post-) fully repeated measures ANOVA ($\alpha = 0.05$). For the majority of our dependent variables, mean values were used in our ANOVA models given that data were not skewed ($g_1 < 0.75$); however, RT data were positively skewed ($g_1 > 1.00$) and as a result medians were used.

Where appropriate, Huynh-Feldt corrections for violations of sphericity are reported (i.e., degrees of freedom adjusted to one decimal place). All interactions and appropriate main effects were decomposed via simple-effects (i.e., reduced model ANOVA and/or paired-samples t-test).

3. Results

3.1. Heart rate and blood pressure.

Heart rate produced main effects for condition, $F(1.7, 44.7)=106.25$, $p<0.001$, $\eta_p^2=0.80$, time, $F(1.7, 46.1)=28.52$, $p<0.001$, $\eta_p^2=0.51$, and a condition by time interaction, $F(2.2, 59.5)=29.49$, $p<0.001$, $\eta_p^2=0.52$. Passive exercise and control condition heart rates did not vary across the 2- (passive: 83, SD=12, control: 75, SD=8), 12- (passive: 82, SD=12, control: 76, SD=8) and 22-min (passive: 82, SD=11, control: 76, SD=8) intervals (all $t(27)<1.16$ and <-0.98, $ps=0.26$ and $=0.33$, $d_z<0.22$ and < -0.19), whereas active exercise condition heart rates increased from the 2- (98, SD=18) to 12-min (113, SD=20) interval ($t(27)= -5.73$, $p<0.001$, $d_z= -1.08$) and the latter did not differ from the 22-min (115, SD=17) interval ($t(27)= -0.88$, $p=0.39$, $d_z= -0.17$).

Systolic and diastolic blood pressure yielded main effects of condition, all $F(2, 54)=21.59$ and 5.86, $ps<0.001$ and 0.004, $\eta_p^2=0.35$ and 0.13. For systolic blood pressure, passive (127 mmHg, SD=15) and active (145 mmHg, SD=18) exercise conditions produced larger values than the control condition (121 mmHg, SD=8) (all $t(27)> -2.42$, $ps<0.02$, all $d_z> -0.46$), with values in the active exercise condition being larger than the passive exercise condition ($t(27)= -5.88$, $p<0.001$, $d_z= -1.11$). For diastolic blood pressure, active exercise condition values (88 mmHg, SD=11) were larger than control (81 mmHg, SD=8) and passive exercise (82 mmHg, SD=8) conditions (all $t(27)> -2.51$, $ps<0.02$, all $d_z> -0.47$) and the latter two conditions did not reliably differ ($t(27)= -0.28$, $p=0.78$, $d_z= -0.05$).

3.2. *TCD blood flow velocity through the MCA*.

Systolic BV produced main effects for condition, $F(1.8, 49.3)=5.17$, $p=0.009$, $\eta_p^2=0.16$, and time, $F(1, 27)=103.87$, $p<0.001$, $\eta_p^2=0.79$, and their interaction, $F(1.7, 46.8)=53.26$, $p<0.001$, $\eta_p^2=0.66$. **Figure 3** demonstrates that passive and active exercise conditions increased BV from

baseline to steady-state (all t(27)= -5.33 and -9.98, ps<0.001, d_z= -1.01 and -1.89), whereas no reliable change from baseline was observed for the control condition (t(27)=0.57, p=0.57, d_z=0.11). To address whether the magnitude of the baseline to steady-state change in BV varied across active and passive exercise conditions we computed participant-specific BV difference scores (i.e., steady-state minus baseline) and observed that values were larger in the active (25 cm/s, SD=13) than passive (7cm/s, SD=7) exercise condition (t(27)= -6.81, p<0.001, d_z= -1.29).

3.3. Oculomotor performance.

RT produced a main effect for time, $F(1, 27)=20.67$, p<0.001, $\eta_p^2=0.43$, and a condition by time interaction, $F(2, 54)=10.64$, p<0.001, $\eta_p^2=0.28$. **Figure 4a** shows that control condition RTs did not reliably vary pre- to post-condition (t(27)= -0.19, p=0.85, d_z= -0.04), whereas passive and active condition RTs decreased postexercise (all t(27)=2.23 and 5.75, ps=0.034 and <0.001, d_z=0.42 and 1.09). Given the nature of our research objective, we computed active and passive exercise condition RT difference scores (i.e., post- minus pre-condition) and **Figure 4b** shows a larger magnitude reduction in the former (t(27)=2.14, p=0.042, d_z=0.40).

RT IQR yielded a main effect of condition, $F(2, 54)=3.80$, p=0.03, $\eta_p^2=0.12$: passive exercise condition RTs (49 ms, SD=18) were more variable than control (43 ms, SD=14) or active exercise (44 ms, SD=16) conditions (all t(27)= -2.59 and 2.11, ps=0.02 and 0.044, d_z= -0.48 and 0.39), and the latter two conditions did not reliably differ (t(27)= -0.58, p=0.57, d_z= -0.11).

The grand means for saccade duration and saccade gain were 64 ms (SD=19) and 0.74° (SD=0.22), respectively, and neither variable elicited reliable main effects or interactions, all $F(1,27)<3.85$, ps>0.06, $\eta_p^2<0.13$.

3.4. Correlation of steady-state BV and antisaccade RT in active and passive exercise conditions

A Pearson r correlation for the active exercise condition indicated that steady-state BVs increased with decreasing post-exercise antisaccade RTs ($p=.049$), whereas for the passive condition the relationship approached – but did not attain – a conventional level of significance ($p=.081$).

4. Discussion

We sought to determine if passive exercise increases CBF and relates to a postexercise benefit to executive function, and we examined whether the magnitude of a putative executive function benefit for passive exercise is comparable to active exercise. In outlining our findings, we first describe results for the active exercise condition before turning to the hemodynamic and executive function findings in the passive exercise condition.

4.1. The metabolic demands of active exercise increase CBF and decrease antisaccade RTs.

The active exercise condition entailed 20-min of volitional cycling and produced a baseline to steady-state increase in HR, blood pressure (systolic and diastolic) and BV. These findings correspond to the well-documented cardio- and neurovascular changes mediating the increased metabolic demands of active exercise (for reviews see Lavie et al., 2015; Smith & Ainslie, 2017). In line with these changes, the oculomotor assessment showed a postexercise reduction in antisaccade RTs. The decrease in antisaccade RTs cannot be attributed to a practice-related effect given that values in the non-exercise control condition did not vary from pre- to post-assessment. Moreover, that saccade duration and gain did not vary pre- to postexercise indicates that the RT reduction was unrelated to an explicit or implicit strategy designed to reduce planning times to enhance response accuracy (i.e., so-called speed-accuracy trade-off) (Fitts, 1954). Instead, the RT findings support a myriad of studies reporting that a single bout of active exercise elicits a short-term "boost" to executive function networks (for meta-analyses see Chang et al., 2012; Lambourne & Tomproroski, 2010; Ludyga et al., 2016; see also Renke et al., 2022). As well, the increase in BV *during* the active exercise condition – and not the non-exercise control condition – suggests that an exercise-mediated increase in CBF may support improved

executive function (Kleinloog et al., 2019; Tari et al., 2020; for review of cerebral hypoperfusion and executive function see Poels et al., 2008).

One issue to address in the active exercise condition is that the work-rate was set at a light intensity (i.e., 37 W). This is a notable because the inverted-U theory asserts that moderate-intensity exercise benefits executive function, whereas light- and heavy-intensities elicit a smaller, null, or negative effect (see Chang et al., 2012; Chang & Etnier, 2009; Tsukamoto et al., 2017). In reconciling this issue, studies have typically used a percentage of participants' $\dot{V}O_{2peak/max}$ in determining intensity – a potential limitation given that $\dot{V}O_2$ and power output are not linearly related (for review Keir et al., 2018). As such, exercise intensity determined via a percentage of $\dot{V}O_{2peak/max}$ does not provide participant-specific equivalence in determining a dose-response relationship across the continuum of metabolically sustainable work rates. More recent work by our group employed lactate threshold (LT) in determining participant-specific work rates across light- (i.e., 25 W), moderate- (80% of participant-specific LT), heavy- (15% of the difference between participants' estimated LT and $\dot{V}O_{2peak}$) and very-heavy- (50% of the difference between participants' estimated LT and $\dot{V}O_{2peak}$) intensity exercise. As expected, ventilatory ($\dot{V}_E$) and gas exchange ($\dot{V}O_2$, $\dot{V}CO_2$, $P_{ET}CO_2$) variables increased across the light- to very-heavy intensities, as did cortical hemodynamics measured via TCD and near-infrared spectroscopy (Heath et al., 2018; Petrella et al., 2019; Tari et al., 2021a). In particular, Tari et al. reported that light-, moderate- and heavy-intensity work rates produced an average baseline to steady-state increase in BV of 22 cm/s, 32 cm/s, and 46 cm/s, respectively. In spite of the scaling of BV to exercise intensity, null hypothesis, equivalence testing and Bayesian evaluation of the null hypothesis indicated that the magnitude of a postexercise benefit to antisaccade RTs did not vary with exercise intensity (see also Dirk et al., 2020; Heath et al., 2018; Petrella et al.,

2019). Additionally, in the present work we used independent samples t-tests to contrast active exercise condition baseline to steady-state changes in BV and postexercise antisaccade RT difference scores to those reported in Tari et al.'s (2021a) light-intensity condition. Results showed that between-experiment BV and RT values did not reliably differ (ts(42)=0.94 and 1.45, ps=0.37 and 0.14, d_z=0.28 and 0.46). In other words, findings evince that active light intensity exercise provides sufficient reactivity to elicit a consistent magnitude postexercise benefit to an oculomotor-based index of executive function.

4.2. Passive exercise increases CBF and decreases antisaccade RTs independent of task-based ventilatory and metabolic demands

The present work included a procedural validation to determine if the passive cycle ergometry used here resulted in volitional activation of agonist musculature and increased ventilatory and metabolic demands. As mentioned previously, we deemed the procedural validation as necessary given that some work has shown that passive exercise produces an early increase in ventilation and steady-state hyperpnea (e.g., Bell & Duffin, 2004). In our passive exercise condition, EMG of the vastus lateralis (i.e., primary agonist in leg extension) did not show periodized activation during the extension phase of each pedal stroke and produced an activation pattern on par to the non-exercise control condition. As well, the passive exercise and control conditions did not elicit baseline to steady-state changes in $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$ or heart rate. In contrast, the active exercise condition showed periodized activation of the vastus lateralis and this activation was associated with a robust increase in $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$, blood pressure and heart rate. The procedural validation therefore demonstrated that the passive exercise protocol (i.e., cycle ergometer with mechanical flywheel and metronome-specified cadence) provided a basis

to evaluate whether a change in BV independent of the metabolic demands of active exercise support a postexercise improvement in antisaccade RTs.

In our main experiment, passive exercise and control condition interventions did not produce a change in heart rate or diastolic blood pressure, whereas in the active exercise condition the aforementioned values reliably increased from baseline to steady-state. It is, however, important to recognize that both active *and* passive exercise conditions – but not the control condition – produced a baseline to steady-state increase in BV; albeit the magnitude of the increase was larger in the active (25 cm/s) than passive (7 cm/s) exercise condition. The increased BV in the active exercise condition reflects increased volumetric CBF arising from increased O_2 delivery (Hoiland et al., 2019) and is a well-defined consequence of the metabolic demands of volitional muscle activation in continuous aerobic exercise (Smith & Ainslie, 2017). In turn, results for the passive exercise condition are in line with work showing that involuntary movement of the limbs results in an increase in CBF. For example, Nagaya et al. (2015) had participants complete 1-min sessions of active and passive (via clinician manipulation) ankle plantar- and dorsiflexion and found that both conditions produced a baseline to steady-state increase in CBF with the magnitude of the increase being larger in the active condition. As well, Doering et al. (1998) showed that 20 s sessions of passive and active flexion/extension of the upper- and lower-limbs increased CBF (but see Sato et al., 2009). The basis for the increased CBF during passive exercise is thought to reflect: (1) increased discharge frequency of mechanosensitive Group III muscle afferents (so-called ergoreceptors) that stimulate brain stem (Aman, 2012) and primary somatosensory cortex (Gladwell & Coote, 2002) neurons supporting cerebral autoregulation, and (2) feedforward signals from primary and supplementary motor areas to the autonomic nervous system (Asahara et al., 2018; Eldridge et al., 1985; Goodwin et

al., 1972; Krogh & Lindhard, 1913; Matsukawa, 2012; Victor et al., 1995). In spite of the different mechanisms associated with the increase in CBF, both active and passive exercise conditions produced a pre- to postexercise decrease in antisaccade RTs with a larger magnitude reduction in the former condition. As well, correlations indicated that steady-state BV related to the magnitude of active and passive condition post-exercise antisaccade RTs. As such, our results provide a first demonstration that passive exercise benefits an oculomotor-based index of executive function and evince that an increase in CBF independent of the metabolic costs of active exercise relates – and possibly contributes – to this improvement (i.e., the hemo-neural hypothesis: Moore & Cao, 2008).

At least two issues require addressing. The first relates to the fact that passive exercise increased systolic blood pressure without concomitant changes in diastolic blood pressure, heart rate, gas exchange and ventilatory measures. The basis for these results can be drawn from the so-called "muscle pump" effect wherein passive exercise increases venous return and increases stroke volume and cardiac output without influencing heart rate (Lujan & DiCarlo, 2014; Trinity et al., 2010). The second issue relates to the larger postexercise reduction in antisaccade RTs in the active than passive exercise condition. This represents an unexpected finding given previous work by our group showing that intensity-specific modulations in an active exercise intervention do not impart additive CBF-executive function benefits (Tari et al., 2021a). In considering this issue, we note that the change in BV for the passive exercise condition (7 cm/s) was smaller than that associated with the active exercise condition (25 cm/s), and the light-intensity condition (22 cm/s) used by Tari et al. (2021a). Given these findings there may be a minimum threshold by which an increase in CBF imparts a non-additive benefit to the oculomotor-based measure of executive function used here.

4.3. Study limitations

We recognize the present work is limited by a number of methodological constraints. First, we used a single active and passive exercise duration (i.e., 20-min) and evaluated postexercise executive function at one time point (i.e., immediately postexercise). As a result, it is unclear whether shorter or longer passive exercise durations similarly benefit antisaccade RTs, and it is entirely unclear for how long a passive exercise executive function benefit persists. Indeed, in active exercise, an executive function benefit can persist up to 60-min postexercise (Joyce et al., 2009; Hung et al., 2013; Shukla & Heath, 2021; but see Chang et al., 2012). Hence, it would be informative to examine whether a passive exercise benefit exhibits the same temporal persistence as its active exercise counterpart. Second, our results are specific to healthy young adults and cannot be directly extended to older populations or those with compromised CBF given that such groups exhibit distinct reactivity to active and passive exercise (McLeod & Stromhaug, 2017; see also, Ludyga et al., 2016). Third, a change in BV measured via TCD does not take into consideration vessel diameter. This represents a possible limitation because under specific physiological conditions the MCA is capable of dilation and constriction (Coverdale et al., 2015); however, to our knowledge such changes have not been shown to influence the validity of TCD in evaluating exercise-mediated MCA changes in BV. Fourth, a single bout postexercise benefit to executive function has not only been linked to increased CBF but also an increase in biomolecule concentrations (i.e., brain-derived neurotrophic factor, catecholamines, serotonin) (Knaepen et al., 2010; Zouhal et al., 2008) and enhanced resting state functional connectivity within frontoparietal networks (e.g., Voss et al., 2010). Accordingly, we are unable to conclude directly that an increase in CBF selectively elicited the observed benefit to executive function following passive and active exercise. Regardless of the aforementioned limitations, we believe

the present findings add importantly to the literature insomuch as they provide a first demonstration that a 20-min single bout of passive exercise increases CBF and improves an oculomotor-based measure of executive function in healthy young adults. Such results provide not only an improved direction for understanding the mechanism by which exercise benefits executive function, but also supports a potential clinical understanding that individuals with reduced mobility (e.g., spinal cord injury) may accrue transient and additive benefits to brain health via passive exercise.

5. References

Amann, M. (2012). Significance of Group III and IV muscle afferents for the endurance exercising human. Clinical and Experimental Pharmacology and Physiology, 39(9), 831-835. https://doi.org/10.1111/j.1440-1681.2012.05681.x

Asahara, R., & Matsukawa, K. (2018). Decreased prefrontal oxygenation elicited by stimulation of limb mechanosensitive afferents during cycling exercise. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 315(2), R230-R240. https://doi.org/10.1152/ajpregu.00454.2017

Barella, L. A., Etnier, J. L., & Chang, Y. K. (2010). The immediate and delayed effects of an acute bout of exercise on cognitive performance of healthy older adults. Journal of Aging and Physical Activity, 18(1), 87-98. https://doi.org/10.1123/japa.18.1.87

Bertsch, K., Hagemann, D., Hermes, M., Walter, C., Khan, R., & Naumann, E. (2009). Resting cerebral blood flow, attention, and aging. Brain research, 1267, 77-88. https://doi.org/10.1016/j.brainres.2009.02.053

Bell, H.J., & Duffin, J. (2004). Rapid increases in ventilation accompany the transition from passive to active movement. Respiratory Physiology & Neurobiology, 152(2), 128-142. https://doi.org/10.1016/j.resp.2005.07.008

Bell, H.J., & Duffin, J. (2003). The respiratory response to passive limb movement is suppressed by a cognitive task. European Journal of Applied Physiology, 97(6), 2112-2120. https://doi.org/10.1152/japplphysiol.00302.2004

Bell, H. J., & Duffin, J. (2006). Rapid increases in ventilation accompany the transition from passive to active movement. Respiratory Physiology & Neurobiology, 152(2), 128–142. https://doi.org/10.1016/j.resp.2005.07.008

Bell, H.J., Ramsaroop, D.M., & Duffin, J. (2003). The respiratory effects of two modes of passive exercise. European Journal of Applied Physiology, 88(6), 544-552. https://doi.org/10.1007/s00421-002-0771-5

Bishop, C. C., Powell, S., Rutt, D., & Browse, N. L. (1986). Transcranial Doppler measurement of middle cerebral artery blood flow velocity: a validation study. Stroke, 17(5), 913-915. https://doi.org/10.1161/01.STR.17.5.913

Brainard, D. H., & Vision, S. (1997). The psychophysics toolbox. Spatial vision, 10(4), 433-436. https://doi.org/10.1163/156856897X00357

Chang, Y. K., & Etnier, J. L. (2009). Exploring the dose-response relationship between resistance exercise intensity and cognitive function. Journal of Sport and Exercise Psychology, 31(5), 640-656. https://doi.org/10.1123/jsep.31.5.640

Chang, Y. K., Labban, J. D., Gapin, J. I., & Etnier, J. L. (2012). The effects of acute exercise on cognitive performance: a meta-analysis. Brain research, 1453, 87-101. https://doi.org/10.1016/j.brainres.2012.02.068

Clyde, B. L., Resnick, D. K., Yonas, H., Smith, H. A., & Kaufmann, A. M. (1996). The relationship of blood velocity as measured by transcranial doppler ultrasonography to cerebral blood flow determined by stable xenon computed tomographic as studies after aneurysmal subarachnoid hemorrhage. Neurosurgery, 38(5), 896-905. https://doi.org/10.1097/00006123-199605000-00008

Colcombe, S. J., Kramer, A. F., McAuley, E., Erickson, K. I., & Scalf, P. (2004). Neurocognitive aging and cardiovascular fitness. Journal of molecular neuroscience, 24(1), 9-14. https://doi.org/10.1385/JMN:24:1:009

Cornelissen, F. W., Peters, E. M., & Palmer, J. (2002). The Eyelink Toolbox: eye tracking with MATLAB and the Psychophysics Toolbox. Behavior Research Methods, Instruments, & Computers, 34(4), 613-617. https://doi.org/10.3758/BF03195489

Coverdale, N. S., Lalande, S., Perrotta, A., & Shoemaker, J. K. (2015). Heterogeneous patterns of vasoreactivity in the middle cerebral and internal carotid arteries. American Journal of Physiology-Heart and Circulatory Physiology, 308(9), H1030-H1038. https://doi.org/10.1152/ajpheart.00761.2014

Cumming, G., (2014). The new statistics: Why and how. Psychological Science, 25 (1), 7-29.

Dafoe, J. M., Armstrong, I. T., & Munoz, D. P. (2007). The influence of stimulus direction and eccentricity on pro-and anti-saccades in humans. Experimental Brain Research, 179(4), 563-570. https://doi.org/10.1007/s00221-006-0817-8

DeSimone, J. C., Weiler, J., Aber, G. S., & Heath, M. (2014). The unidirectional prosaccade switch-cost: correct and error antisaccades differentially influence the planning times for subsequent prosaccades. Vision research, 96, 17-24. https://doi.org/10.1016/j.visres.2013.12.005

Diamond, A. (2013). Executive functions. Annual review of psychology, 64, 135-168. https://doi.org/10.1146/annurev-psych-113011-143750

Dirk, K. L., Belfry, G. R., & Heath, M. (2020). Exercise and executive function during follicular and luteal menstrual cycle phases. Medicine and Science in Sports and Exercise, 52(4), 919-927. https://doi.org/10.1249/mss.0000000000002192

Doering, T. J., Resch, K. L., Steuernagel, B., Brix, J., Schneider, B., & Fischer, G. C. (1998). Passive and active exercise increase cerebral blood flow velocity in young, healthy individuals1. American journal of physical medicine & rehabilitation, 77(6), 490-493. https://doi.org/10.1097/00002060-199811000-00006

Doherty, C. J., Incognito, A. V., Notay, K., Burns, M. J., Slysz, J. T., Seed, J. D., ... & Millar, P. J. (2018). Muscle sympathetic nerve responses to passive and active one-legged cycling: insights into the contributions of central command. American Journal of Physiology-Heart and Circulatory Physiology, 314(1), H3-H10. https://doi.org/10.1152/ajpheart.00494.2017

Duschek, S., Hoffmann, A., Montoro, C. I., Del Paso, G. A. R., Schuepbach, D., & Ettinger, U. (2018). Cerebral blood flow modulations during preparatory attention and proactive inhibition. Biological Psychology, 137, 65-72. https://doi.org/10.1016/j.biopsycho.2018.07.003

Eldridge, F. L., Millhorn, D. E., Killey, J. P., & Waldrop, T. G. (1985). Stimulation by central command of locomotion, respiration and circulation during exercise. Respiration physiology, 59(3), 313-337. https://doi.org/10.1016/0034-5687(85)90136-7

Everling, S., & Johnston, K. (2013). Control of the superior colliculus by the lateral prefrontal cortex. Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 368 (1628), 20130068. https://doi.org/10.1098/rstb.2013.0068

Fischer, B., & Weber, H. (1992). Characteristics of "anti" saccades in man. Experimental Brain Research, 89(2), 415-424. https://doi.org/10.1007/BF00228257

Fitts, P. M. (1954). The information capacity of the human motor system in controlling the amplitude of movement. Journal of experimental psychology, 47(6), 381. https://doi.org/10.1037/h0055392

Gillen, C., & Heath, M. (2014). Perceptual averaging governs antisaccade endpoint bias. Experimental brain research, 232(10), 3201-3210. https://doi.org/10.1007/s00221-014-4010-1

Gladwell, V. F., & Coote, J. H. (2002). Heart rate at the onset of muscle contraction and during passive muscle stretch in humans: a role for mechanoreceptors. The Journal of physiology, 540(3), 1095-1102. https://doi.org/10.1113/jphysiol.2001.013486

Goodwin, G. M., McCloskey, D. I., & Mitchell, J. H. (1972). Cardiovascular and respiratory responses to changes in central command during isometric exercise at constant muscle tension. The Journal of physiology, 226(1), 173-190. https://doi.org/10.1113/jphysiol.1972.sp009979

Hallett, P. E. (1978). Primary and secondary saccades to goals defined by instructions. Vision research, 18(10), 1279-1296. https://doi.org/10.1016/0042-6989(78)90218-3

Heath, M., & Shukla, D. (2020). A single bout of aerobic exercise provides an immediate "boost" to cognitive flexibility. Frontiers in Psychology, 11, 1106. https://doi.org/10.3389/fpsyg.2020.01106

Heath, M., Petrella, A., Blazevic, J., Lim, D., Pelletier, A., & Belfry, G. R. (2018). A post-exercise facilitation of executive function is independent of aerobically supported metabolic costs. Neuropsychologia, 120, 65-74. https://doi.org/10.1016/j.neuropsychologia.2018.10.002

Heath, M., Weiler, J., Gregory, M. A., Gill, D. P., & Petrella, R. J. (2016). A six-month cognitive-motor and aerobic exercise program improves executive function in persons with an objective cognitive impairment: a pilot investigation using the antisaccade task. Journal of Alzheimer's Disease, 54(3), 923-931. https://doi.org/10.3233/JAD-160288

Hoiland, R. L., Fisher, J. A., & Ainslie, P. N. (2011). Regulation of the cerebral circulation by arterial carbon dioxide. Comprehensive Physiology, 9(3), 1101-1154. https://doi.org/10.1002/cphy.c180021

https://doi.org/10.1177/0956797613504966.

Hug, F., & Dorel, S. (2009). Electromyographic analysis of pedaling: a review. Journal of electromyography and Kinesiology, 19(2), 182-198. https://doi.org/10.1016/j.jelekin.2007.10.010

Hung, T. M., Tsai, C. L., Chen, F. T., Wang, C. C., & Chang, Y. K. (2013). The immediate and sustained effects of acute exercise on planning aspect of executive function. Psychology of Sport and Exercise, 14(5), 728-736. https://doi.org/10.1016/j.psychsport.2013.05.004

Ito, H., Kanno, I., Ibaraki, M., Hatazawa, J., & Miura, S. (2003). Changes in human cerebral blood flow and cerebral blood volume during hypercapnia and hypocapnia measured by positron emission tomography. Journal of Cerebral Blood Flow & Metabolism, 23(6), 665-670. https://doi.org/10.1097/01.WCB.0000067721.64998.F5

Joyce, J., Graydon, J., McMorris, T., & Davranche, K. (2009). The time course effect of moderate intensity exercise on response execution and response inhibition. Brain and cognition, 71(1), 14-19. https://doi.org/10.1016/j.bandc.2009.03.004

Keir, D. A., Paterson, D. H., Kowalchuk, J. M., & Murias, J. M. (2018). Using ramp-incremental $\dot{V}O_2$ responses for constant-intensity exercise selection. Applied Physiology, Nutrition, and Metabolism, 43(9), 882-892. https://doi.org/10.1139/apnm-2017-0826

Kety, S. S., & Schmidt, C. F. (1948). The nitrous oxide method for the quantitative determination of cerebral blood flow in man: theory, procedure and normal values. The Journal of clinical investigation, 27(4), 476-483. https://doi.org/10.1172/JCI101994

Kleiner, M., Brainard, D., & Pelli, D. (2007). What's new in Psychtoolbox-3?. https://doi.org/10.1177/03010066070360S101

Kleinloog, J. P., Mensink, R. P., Ivanov, D., Adam, J. J., Uludağ, K., & Joris, P. J. (2019). Aerobic exercise training improves cerebral blood flow and executive function: a randomized, controlled cross-over trial in sedentary older men. Frontiers in aging neuroscience, 333. https://doi.org/10.3389/fnagi.2019.00333

Knaepen, K., Goekint, M., Heyman, E. M., & Meeusen, R. (2010). Neuroplasticity—exercise-induced response of peripheral brain-derived neurotrophic factor. Sports medicine, 40(9), 765-801. https://doi.org/10.2165/11534530

Krogh, A., & Lindhard, J. (1913). The regulation of respiration and circulation during the initial stages of muscular work. The Journal of physiology, 47(1-2), 112. https://doi.org/10.1113/jphysiol.1913.sp001616

Lakens, D., Scheel, A. M., & Isager, P. M. (2018). Equivalence testing for psychological research: A tutorial. Advances in Methods and Practices in Psychological Science, 1(2), 259-269. https://doi.org/10.1177/2515245918770963

Lambourne, K., & Tomporowski, P. (2010). The effect of exercise-induced arousal on cognitive task performance: a meta-regression analysis. Brain research, 1341, 12-24. https://doi.org/10.1016/j.brainres.2010.03.091

Lavie, C. J., Arena, R., Swift, D. L., Johannsen, N. M., Sui, X., Lee, D. C., ... & Blair, S. N. (2015). Exercise and the cardiovascular system: clinical science and cardiovascular outcomes. Circulation research, 117(2), 207-219. https://doi.org/10.1161/CIRCRESAHA.117.305205

Ludyga, S., Gerber, M., Brand, S., Holsboer-Trachsler, E., & Pühse, U. (2016). Acute effects of moderate aerobic exercise on specific aspects of executive function in different age and fitness groups: A meta-analysis. Psychophysiology, 53(11), 1611-1626. https://doi.org/10.1111/psyp.12736

Lujan, H. L., & DiCarlo, S. E. (2014). Increasing venous return as a strategy to prevent or reverse cardiac dysfunction following spinal cord injury. The Journal of Physiology, 592(Pt 8), 1727. https://doi.org/10.1113/jphysiol.2014.272666

Matsukawa, K. (2012). Central command: control of cardiac sympathetic and vagal efferent nerve activity and the arterial baroreflex during spontaneous motor behaviour in animals. Experimental Physiology, 97(1), 20-28. https://doi.org/10.1113/expphysiol.2011.057661

Matteis, M., Vernieri, F., Troisi, E., Pasqualetti, P., Tibuzzi, F., Caltagirone, C., & Silvestrini, M. (2003). Early cerebral hemodynamic changes during passive movements and motor recovery after stroke. Journal of neurology, 250(7), 810-817. https://doi.org/10.1007/s00415-003-1082-4

McDaniel, J., Hayman, M. A., Ives, S., Fjeldstad, A. S., Trinity, J. D., Wray, D. W., & Richardson, R. S. (2010). Attenuated exercise induced hyperaemia with age: mechanistic insight from passive limb movement. The Journal of physiology, 588(22), 4507-4517. https://doi.org/10.1113/jphysiol.2010.198770

McLeod, K. J., & Stromhaug, A. (2017). Reversal of cognitive impairment in a hypotensive elderly population using a passive exercise intervention. Clinical Interventions in Aging, 12, 1859. https://doi.org/10.2147/CIA.S147959

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. Cognitive psychology, 41(1), 49-100. https://doi.org/10.1006/cogp.1999.0734

Moore, C. I., & Cao, R. (2008). The hemo-neural hypothesis: on the role of blood flow in information processing. Journal of Neurophysiology, 99(5), 2035-2047. https://doi.org/10.1152/jn.01366.2006

Munoz, D. P., & Everling, S. (2004). Look away: the anti-saccade task and the voluntary control of eye movement. Nature Reviews Neuroscience, 5(3), 218-228. https://doi.org/10.1038/nrn1345

Nagaya, S., Hayashi, H., Fujimoto, E., Maruoka, N., & Kobayashi, H. (2015). Passive ankle movement increases cerebral blood oxygenation in the elderly: an experimental study. BMC Nursing, 14(1), 1-7. https://doi.org/10.1186/s12912-015-0066-x

Nobrega, A. C., & Araujo, C. G. (1993). Heart rate transient at the onset of active and passive dynamic exercise. Medicine and Science in Sports and Exercise, 25(1), 37-41. https://doi.org/10.1249/00005768-199301000-00007

Nobrega, A. C., Williamson, J. W., Friedman, D. B., Araujo, C. G., & Mitchell, J. H. (1994). Cardiovascular responses to active and passive cycling movements. Medicine and Science in Sports and Exercise, 26(6), 709-714. https://doi.org/10.1249/00005768-199406000-00009

Nurhayati, Y. A. T. I., & Boutcher, S. H. (1998). Cardiovascular response to passive cycle exercise. Medicine and Science in Sports and Exercise, 30(2), 234-238. https://doi.org/10.1097/00005768-199802000-00010

Petrella, A. F., Belfry, G., & Heath, M. (2019). Older adults elicit a single-bout post-exercise executive benefit across a continuum of aerobically supported metabolic intensities. Brain Research, 1712, 197-206. https://doi.org/10.1016/j.brainres.2019.02.009

Poels, M. M., Ikram, M. A., Vernooij, M. W., Krestin, G. P., Hofman, A., Messen, W. J., ... & Breteler, M. M. (2008). Total cerebral blood flow in relation to cognitive function: the Rotterdam Scan Study. Journal of Cerebral Blood Flow & Metabolism, 28(10), 1652-1655. https://doi.org/10.1038/jcbfm.2008.62

Raper, A. J., Kontos, H. A., & Patterson Jr, J. L. (1971). Response of pial precapillary vessels to changes in arterial carbon dioxide tension. Circulation Research, 28(5), 518-523. https://doi.org/10.1161/01.RES.28.5.518

Renke, M. B., Marcinkowska, A. B., Kujach, S., & Winklewski, P. J. (2022). A systematic review of the impact of physical exercise-induced increased resting cerebral blood flow on cognitive functions. Front. Aging Neurosci. 14: 803332. https://doi.org/10.3389/fnagi.2022.803332

Rosengarten, B., & Kaps, M. (2002). Peak systolic velocity Doppler index reflects most appropriately the dynamic time course of intact cerebral autoregulation. Cerebrovascular Diseases, 13(4), 230-234. https://doi.org/10.1159/000057848

Samani, A., & Heath, M. (2018). Executive-related oculomotor control is improved following a 10-min single-bout of aerobic exercise: Evidence from the antisaccade task. Neuropsychologia, 108, 73-81. https://doi.org/10.1016/j.neuropsychologia.2017.11.029

Sato, K., Moriyama, M., & Sadamoto, T. (2009). Influence of central command on cerebral blood flow at the onset of exercise in women. Experimental Physiology, 94(11), 1139-1146. https://doi.org/10.1113/expphysiol.2009.048587

Shim, C. Y., Park, S., Choi, E. Y., Hong, G. R., Choi, D., Jang, Y., & Chung, N. (2013). The relationship between ventricular-vascular uncoupling during exercise and impaired left ventricular longitudinal functional reserve in hypertensive patients. Journal of the American Society of Hypertension, 7(3), 198-205. https://doi.org/10.1016/j.jash.2013.01.005

Shukla, D., & Heath, M. (2021). A single bout of exercise provides a persistent benefit to cognitive flexibility. Research Quarterly for Exercise and Sport, 1-12. https://doi.org/10.1080/02701367.2021.1873902

Smith, K. J., & Ainslie, P. N. (2017). Regulation of cerebral blood flow and metabolism during exercise. Experimental Physiology, 102(11), 1356-1371. https://doi.org/10.1113/EP086249

Takata, T., Yamabe, H., & Fukuzaki, H. (1990). The role of oxygen extraction in peripheral tissues in exercise capacity in chronic heart failure. Japanese journal of Medicine, 29(3), 266-273. https://doi.org/10.2169/internalmedicine1962.29.266

Tari, B., Shirzad, M., Badcock, N. A., Belfry, G. R., & Heath, M. (2021b). 'Delaying' a saccade: Preparatory phase cortical hemodynamics evince the neural cost of response inhibition. Brain and Cognition, 154, 105808. https://doi.org/10.1016/j.bandc.2021.105808

Tari, B., Shirzad, M., Behboodpour, N., Belfry, G. R., & Heath, M. (2021a). Exercise intensity-specific changes to cerebral blood velocity do not modulate a postexercise executive function benefit. Neuropsychologia, 161, 108018. https://doi.org/10.1016/j.neuropsychologia.2021.108018

Tari, B., Vanhie, J. J., Belfry, G. R., Shoemaker, J. K., & Heath, M. (2020). Increased cerebral blood flow supports a single-bout postexercise benefit to executive function: evidence from hypercapnia. Journal of Neurophysiology, 124(3), 930-940. https://doi.org/10.1152/jn.00240.2020

Terslev, L., Diamantopoulos, A. P., Døhn, U. M., Schmidt, W. A., & Torp-Pedersen, S. (2017). Settings and artefacts relevant for Doppler ultrasound in large vessel vasculitis. Arthritis Research & Therapy, 19(1), 1-10. https://doi.org/10.1186/s13075-017-1374-1

Trinity, J. D., & Richardson, R. S. (2019). Physiological impact and clinical relevance of passive exercise/movement. Sports Medicine, 49(9), 1365-1381. https://doi.org/10.1007/s40279-019-01146-1

Tsukamoto, H., Takenaka, S., Suga, T., Tanaka, D., Takeuchi, T., Hamaoka, T., ... & Hashimoto, T. (2017). Impact of exercise intensity and duration on postexercise executive function.

Medicine and Science in Sports and Exercise, 49(4), 774-784. https://doi.org/10.1249/mss.0000000000001155

Verburgh, L., Königs, M., Scherder, E. J., & Oosterlaan, J. (2014). Physical exercise and executive functions in preadolescent children, adolescents and young adults: a meta-analysis. British journal of sports medicine, 48(12), 973-979. http://dx.doi.org/10.1136/bjsports-2012-091441

Victor, R. G., Secher, N. H., Lyson, T., & Mitchell, J. H. (1995). Central command increases muscle sympathetic nerve activity during intense intermittent isometric exercise in humans. Circulation Research, 76(1), 127-131. https://doi.org/10.1161/01.RES.76.1.127

Voss, M. W., Erickson, K. I., Prakash, R. S., Chaddock, L., Malkowski, E., Alves, H., ... & Kramer, A. F. (2010). Functional connectivity: a source of variance in the association between cardiorespiratory fitness and cognition?. Neuropsychologia, 48(5), 1394-1406. https://doi.org/10.1016/j.neuropsychologia.2010.01.005

Wenban-Smith, M. G., & Findlay, J. M. (1991). Express saccades: is there a separate population in humans?. Experimental Brain Research, 87(1), 218-222. https://doi.org/10.1007/BF00228523

Zouhal, H., Jacob, C., Delamarche, P., & Gratas-Delamarche, A. (2008). Catecholamines and the effects of exercise, training and gender. Sports medicine, 38(5), 401-423. https://doi.org/10.2165/00007256-200838050-00004

Author Notes

This work was supported by a Discovery Grant from the Natural Sciences and Engineering Research Council (NSERC) of Canada; and Faculty Scholar and Major Academic Development Fund Awards from the University of Western Ontario. The authors declare no commercial, financial or other conflict of interest. Reprint requests for this work can be sent to Matthew Heath (mheath2@uwo.ca).

Author Contributions

Mustafa Shirzad: Conceptualization; data curation; methodology; investigation; formal analysis; Writing – Review & Editing. **Benjamin Tari**: Conceptualization; methodology; formal analysis; Writing – Review & Editing. **Connor Dalton**: Investigation; formal analysis. **James Van Riesen**: Investigation; formal analysis. **Michael Marsala**: Investigation; formal analysis. **Matthew Heath**: Conceptualization, methodology, software; formal analysis; funding; supervision; Writing – Original Draft.

Table 1. Heart rate (HR) and blood pressure (systolic pressure: SBP; diastolic pressure: DBP) for the female participant in the procedural validation investigation at discrete timepoints during the control, passive exercise and active exercise conditions.

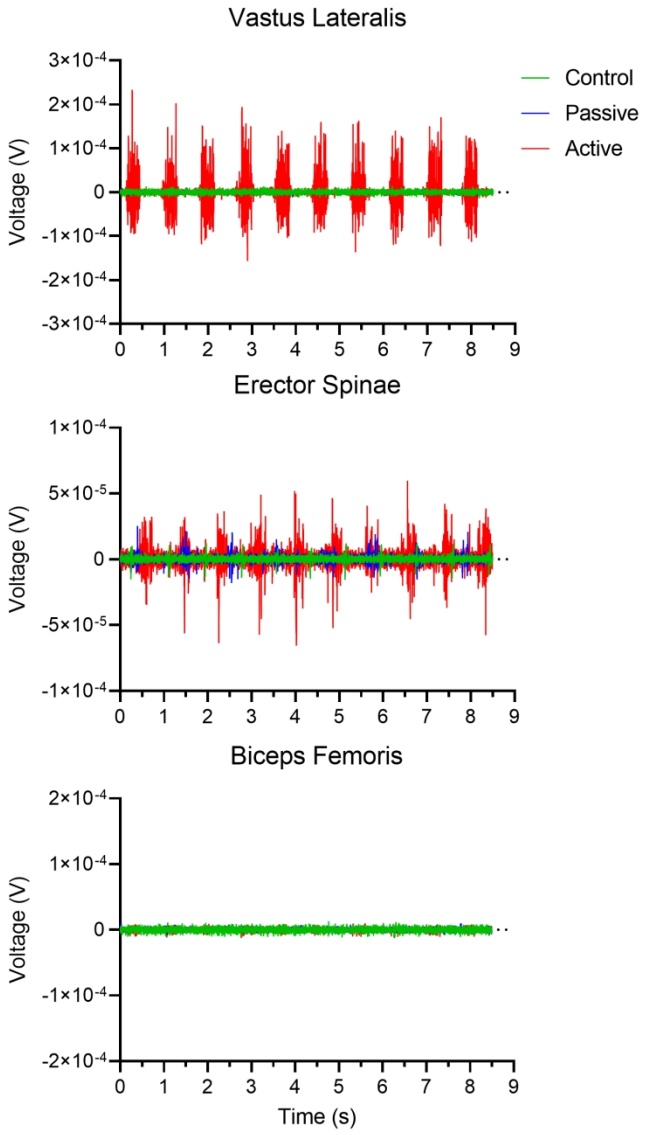
Time (Min)	Control HR	Passive HR	Active HR	Control SBP	Passive SBP	Active SBP	Control DBP	Passive DBP	Active DBP
0	96	92	96	126	124	126	96	94	90
3	92	92	106	120	130	132	96	98	98
6	91	90	124	130	132	142	96	92	98
9	96	96	130	126	136	150	96	88	96
12	94	92	128	124	130	148	94	94	92
15	94	94	132	118	132	142	98	98	96
18	96	96	138	136	136	144	100	92	98
21	96	96	130	126	136	142	100	80	102
24	92	94	134	128	132	148	94	82	98
Average (SD)	94 (2)	93 (2)	124 (14)	126 (5)	132 (4)	141 (8)	96 (2)	90 (6)	96 (4)

Figure Captions

1. Vastus lateralis (A), erector spinae (B), and biceps femoris (C) electromyography (EMG) of the female participant in the active exercise (red), passive exercise (blue) and control (green) conditions of the procedural validation investigation. The figure demonstrates ten successive pedal strokes starting at the 10-min mark of the active and passive exercise conditions and shows an equivalent time frame for the control condition. The figure shows that the primary agonist (i.e., vastus lateralis) involved in leg extension elicited periodized activity during the active exercise condition, whereas periodized activity did not occur in the passive exercise or control conditions.
2. O_2 consumption ($\dot{V}O_2$), CO_2 output ($\dot{V}CO_2$) and ventilation ($\dot{V}_E$) data of the female participant in the active exercise (red), passive exercise (blue) and the control (green) conditions of the procedural validation pilot investigation. Data were sampled at 5 s intervals across a 24-min (i.e., 2-min baseline, 2-min warmup, and 20-min intervention) period and show that the active exercise condition produced a baseline to steady-state increase in $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$, whereas no such change was observed for the passive exercise or control conditions.
3. The central panel depicts an exemplar participant's systolic blood velocity (BV) from the middle cerebral artery sampled during the active exercise (red), passive exercise (blue) and the control (green) conditions of the main experiment. Data from each condition are overlayed and represent BV over a 24-min (i.e., 2-min baseline, 2-min warmup, and 20-min intervention) period. The vertical grey dotted lines represent the onset of warm-up (i.e., 120 s) and the intervention periods (i.e., 240 s), respectively. Offset panels indicate individual mean (top) and group (bottom) difference scores (i.e., steady-state minus

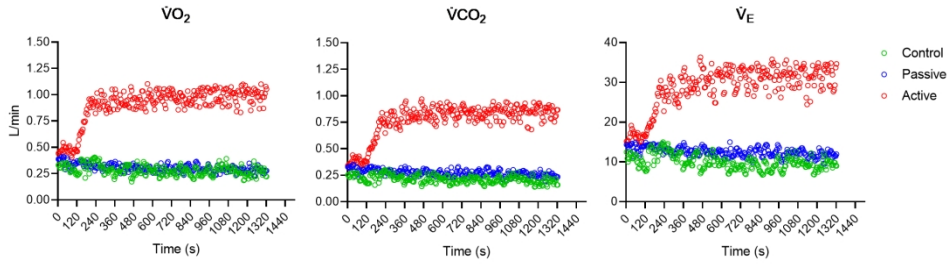
baseline), respectively. The top offset panel includes grey connecting lines to denote participant-specific changes across conditions, and the bottom panel includes 95% between-participant confidence intervals for each condition. In the bottom panel the absence of overlap between the error bar and zero (i.e., horizonal grey line) represents a reliable effect inclusive to a test of the null hypothesis (Cumming, 2014).

4. Panel A depicts participant-specific median pre- and post-condition antisaccade reaction times (RT) for the active exercise (red), passive exercise (blue) and control (green) conditions (Note: pre- and post-conditions values are denoted via open and closed circle symbols, respectively). The solid black lines represent the group mean and associated 95% within-participant confidence intervals. Panel B shows RT difference scores (i.e., post-intervention minus pre-intervention) with error bars representing 95% between-participant confidence intervals during each condition, as well as the mean RT difference score (i.e., passive minus active) between passive and active exercise conditions.



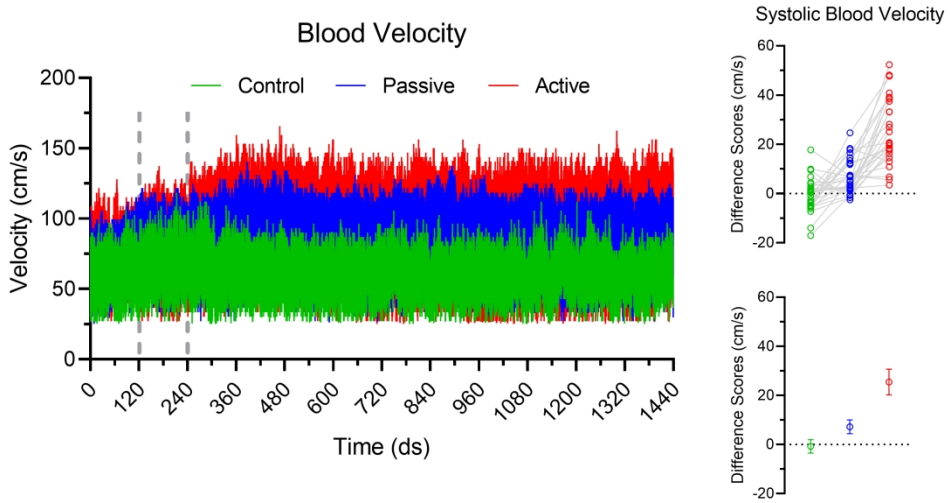
Vastus lateralis (A), erector spinae (B), and biceps femoris (C) electromyography (EMG) of the female participant in the active exercise (red), passive exercise (blue) and control (green) conditions of the procedural validation investigation. The figure demonstrates ten successive pedal strokes starting at the 10-min mark of the active and passive exercise conditions and shows an equivalent time frame for the control condition. The figure shows that the primary agonist (i.e., vastus lateralis) involved in leg extension elicited periodized activity during the active exercise condition, whereas periodized activity did not occur in the passive exercise or control conditions.

134x226mm (300 x 300 DPI)



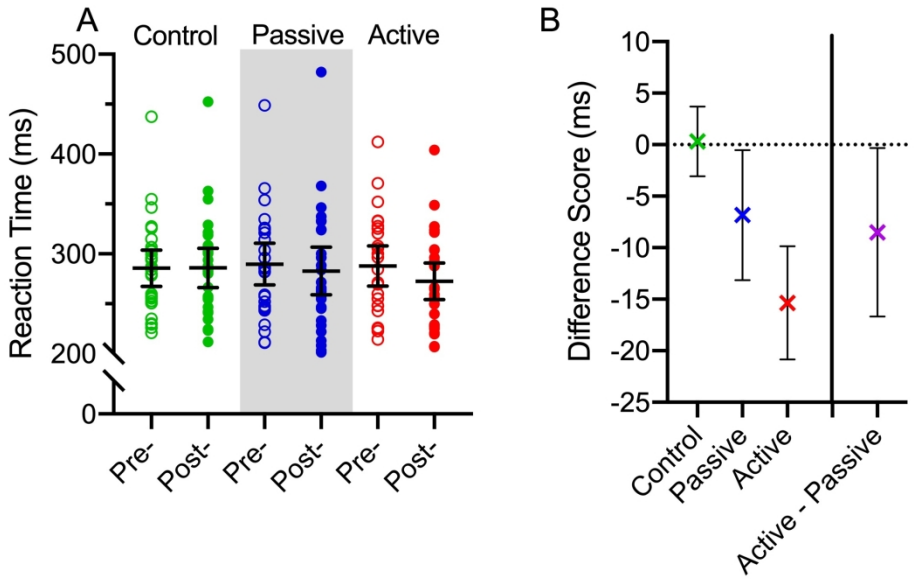
O2 consumption (VO2), CO2 output (VCO2) and ventilation (VE) data of the female participant in the active exercise (red), passive exercise (blue) and the control (green) conditions of the procedural validation pilot investigation. Data were sampled at 5 s intervals across a 24-min (i.e., 2-min baseline, 2-min warmup, and 20-min intervention) period and show that the active exercise condition produced a baseline to steady-state increase in VO2, VCO2 and VE, whereas no such change was observed for the passive exercise or control conditions.

192x60mm (300 x 300 DPI)



The central panel depicts an exemplar participant's systolic blood velocity (BV) from the middle cerebral artery sampled during the active exercise (red), passive exercise (blue) and the control (green) conditions of the main experiment. Data from each condition are overlayed and represent BV over a 24-min (i.e., 2-min baseline, 2-min warmup, and 20-min intervention) period. The vertical grey dotted lines represent the onset of warm-up (i.e., 120 s) and the intervention periods (i.e., 240 s), respectively. Offset panels indicate individual mean (top) and group (bottom) difference scores (i.e., steady-state minus baseline), respectively. The top offset panel includes grey connecting lines to denote participant-specific changes across conditions, and the bottom panel includes 95% between-participant confidence intervals for each condition. In the bottom panel the absence of overlap between the error bar and zero (i.e., horizonal grey line) represents a reliable effect inclusive to a test of the null hypothesis (Cumming, 2014).

266x143mm (300 x 300 DPI)



4. Panel A depicts participant-specific median pre- and post-condition antisaccade reaction times (RT) for the active exercise (red), passive exercise (blue) and control (green) conditions (Note: pre- and post-conditions values are denoted via open and closed circle symbols, respectively). The solid black lines represent the group mean and associated 95% within-participant confidence intervals. Panel B shows RT difference scores (i.e., post-intervention minus pre-intervention) with error bars representing 95% between-participant confidence intervals during each condition, as well as the mean RT difference score (i.e., passive minus active) between passive and active exercise conditions.

214x131mm (300 x 300 DPI)