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A Single-Bout of Aerobic Exercise Improved Executive Control: Evidence From the Antisaccade Task

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Supervisor: Dr. Matthew Heath, The University of Western Ontario A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Kinesiology © Ashna Samani 2017

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Abstract

A single-bout of moderate-to-vigorous intensity exercise increases activity within frontoparietal networks, producing a temporary 'boost' to executive-related cognitive control – an effect that is thought to be selective to exercise durations greater than 20 minutes. It is possible that previous tasks evaluating executive control did not provide the requisite resolution to detect executive changes associated with shorter exercise durations. To that end, I had participants perform a 10 minute bout of moderate-to-vigorous intensity aerobic exercise, examining pre- and postexercise executive control via the antisaccade task. Extensive literature has shown that antisaccades are mediated via frontoparietal networks, modulated following exercise training. Results showed that antisaccade reaction time (RT) decreased by 27 ms from pre- to postexercise assessments, and was a finding shown to be exercise-specific. Accordingly, I propose that a 10-minute single-bout of aerobic exercise increases arousal and activity within executiverelated frontoparietal networks.

Keywords

Aerobic exercise

Antisaccades

Executive control

Oculomotor

Single-bout

Co-Authorship

The author, under the supervision and mentorship of Dr. Matthew Heath, conducted the work in this master's thesis. With the guidance of Dr. Matthew Heath, I designed the experiments, and collected, analyzed, interpreted all of the data, and prepared the manuscript. For this manuscript, Ashna Samani was the first author and Dr. Matthew Heath served as a co-author.

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Introduction

A wealth of evidence has shown that participation in a long-term (i.e., > 6 weeks) aerobic- and/or resistance-based exercise program improves not only general physical health, but also benefits brain health (e.g., Etnier & Landers, 1995). Colcombe and Kramer's (2003) seminal meta-analysis reported that exercise training in healthy young and older (i.e., > 55 years of age) adults produces broad benefits in cognition (e.g., working memory and attention), and more specifically enhances executive-related control. As well, recent work has shown that a 6 month aerobic and/or resistance-based exercise program improves executive control in older adults in the prodromal stages of Alzheimer's disease (Heath, Weiler, Gregory, Gill, & Petrella, 2016b; Heath, Shellington, Titheridge, Gill, & Petrella, 2017). Broadly speaking, executive control relates to an individual's ability to process and attend single and multiple stimuli, update and monitor working memory, and assert high-level inhibitory control (Norman & Shallice, 1986). It is thought that long-term exercise programs improve cognition and executive functioning via a range of neurophysiological changes including: (1) increased levels of brainderived neurotrophic factors (BDNF) that promote neuroplasticity and synaptic efficiency (Cotman & Berchtold, 2002), (2) stimulating hippocampal neurogenesis via cell proliferation (van Praag, Kempermann, & Gage, 1999), and (3) promoting activity, connectivity and density within frontoparietal executive structures (Colcombe, Kramer, Erickson, Scalf, McAuley et al., 2004; Colcombe, Erickson, Scalf, Kim, Prakash et al., 2006; Ruscheweyh, Willemer, Krüger, Duning, Warnecks et al., 2011; Voss, Erickson, Prakash, Chaddock, Malkowski et al., 2010).

In addition to long-term exercise effects, work has examined whether a single-bout of exercise elicits a short-term cognitive 'boost'. Some work has shown that a single-bout of exercise produces a cognitive benefit (e.g., Fleury & Bard, 1987), whereas other studies have not (e.g., Coles & Tomporowski, 2008). Although the results of individual studies are mixed, the meta-analysis by Chang, Labban, Gapin, and Etnier (2012) concluded that a single-bout of exercise (aerobic, resistance, or combined) produces a small but reliable cognitive benefit when the exercise session is performed at a moderate-to-vigorous level of intensity (i.e., 60 – 85% of predicted maximum heart rate; see also Lambourne & Tomporowski, 2010; Etnier, Sibley, Pomeroy, & Kao, 2003). Moreover, Chang et al. (2012) identified that an additional moderator of the single-bout exercise effect was the administration of a task sensitive to addressing

executive-related cognitive processes. Indeed, most early studies examining the single-bout effect employed tasks involving simple reaction time (RT) (Aks, 1998; Fleury & Bard, 1987; McMorris & Keen, 1994), visual recognition (Bard & Fleury, 1978), and working memory (Coles & Tomporowski, 2008), and did not report a reliable cognitive benefit. In turn, more recent work has reported that tasks involving high-level executive functioning elicit a positive exercise benefit (for review see Lambourne & Tomporowski, 2010). For example, Chang et al. (2014) had adult participants (mean age = 58.1 years) perform a single-bout of resistance exercises (e.g., biceps and leg curls at 70% of each participants' 10-repetition maximum) for 20- 25 minutes and evaluated pre- and post-exercise executive control via the Stroop task. In addition, Stroop task performance was assessed in separate sessions interleaved by a 30-minute control condition interval (e.g., participants sat and read). The Stroop task is a speeded reaction time task wherein a series of colour names are printed in ink that is congruent (i.e., standard word-naming task) or incongruent (i.e., non-standard colour-naming task) to the word name. Results consistently report that RTs for the non-standard task are longer – and responses are more errorful – than the standard task, and is a result in part attributed to high-level executive demands related to inhibiting a pre-potent response. Chang et al. (2014) reported that RTs for stimuli-strings were measured via a handheld chronometer and the authors reported that post-test RTs in both exercise and control conditions were shorter than their pre-test counterparts; albeit with the magnitude of the improvement being larger in the exercise (i.e., 22%) than the control (6%) condition. Accordingly, Chang et al. (2014) reported that a single-bout of exercise "…has a more beneficial effect on cognition that involves executive control." (p. 51). In addressing the improved post-exercise performance, Dietrich and Audiffren's (2011) reticular-activating hyperfrontality hypothesis asserts that a single-bout of exercise optimizes physiological and psychological arousal within frontoparietal executive networks and promotes enhanced executive control. In turn, Verburgh, Königs, Scherder, and Oosterlaan (2014) proposed that a single-bout of exercise increases cerebral oxygenation and results in increased regional cerebral blood flow (rCBF) to executive-related cortical structures. Regardless of the precise explanation, convergent evidence suggests that a single-bout of exercise benefits the activity of executiverelated cortical structures.

The positive benefit to executive control outlined in the previous paragraph has been reported to be contingent on the exercise duration. Both Lambourne and Tomporowski's (2010) and Chang et al's (2012) meta-analyses reported that short duration exercise sessions (i.e., <20 minutes) produced a negative or null effect on cognitive and executive performance, whereas durations greater than 20 minutes produced a positive benefit (see also Brisswalter, Collardeau, & René, 2002). Based on this evidence, it was proposed that the physiological changes necessary to promote an executive-related performance benefit require at least 20 minutes of sustained moderate-to-vigorous intensity physical activity. It is, however, important to consider that the duration effect may be influenced by the temporal and spatial precision associated with the equipment and task used to address executive control. Recall that Chang et al's (2014) study employed handheld chronometry to examine exercise related changes to the Stroop task. The measurement precision afforded via handheld chronometry may not provide an accurate basis to detect subtle – yet reliable – changes in executive performance for shorter duration exercise sessions. In addition, the Stroop task and a myriad of other 'executive' tasks (e.g., Tower of London, flanker, visual and acoustic oddball tasks) require not only high-level executive control but also non-executive functions including language, attentional and visuo-spatial analyses. It is therefore possible that the non-executive components associated with the aforementioned tasks preclude an accurate determination of the minimum time required to elicit an exercise-based change in executive control. As such, my thesis work employed the antisaccade task to determine whether a 10-minute single-bout of moderate-to-vigorous intensity aerobic exercise elicits a reliable executive-related performance benefit. The antisaccade task requires that an individual complete a goal-directed eye movement (i.e., a saccade) mirror-symmetrical to the location of a visual stimulus (Hallett, 1978). Extensive behavioural and neuroimaging work from humans as well as electrophysiology from non-human primates has shown that antisaccades are a cognitively challenging and executive-mediated task requiring the suppression of a stimulus-driven response (i.e., response suppression) and the visual remapping of a target's coordinates (i.e., vector inversion) (for review see Munoz & Everling, 2004). Moreover, the performance of directionally correct antisaccades has been linked to increased activation of executive-related frontoparietal networks (Ford, Goltz, Brown, & Everling, 2005; Weiler, Hassall, Krigolson, & Heath, 2015; Zhang & Barash, 2000; for review see Everling & Johnston, 2013) – cortical regions linked to modified activity following a single-bout (Hiura, Mizuno, $\&$ Fujimoto, 2010; Seifert & Secher, 2011) and long-term (Colcombe et al. 2004; Voss et al. 2010) exercise. Thus, the hands- and language-free nature of antisaccades coupled with the temporal

precision of eye-tracking (i.e., 360 Hz in the present investigation) make it an ideal task for determining whether a short-duration single-bout of aerobic exercise benefits executive-related oculomotor control.

Experiment 1 evaluated pro- (i.e., saccade to a veridical target location) and antisaccade performance at pre- and post-exercise assessments. The intervention entailed a single-bout of moderate-to-vigorous intensity aerobic exercise on a cycle ergometer (10 minutes at 60-85% of predicted maximum heart rate with 2.5 minutes each of warm-up and cool-down). In terms of research predictions, if aerobic exercise produces an immediate boost to executive-related oculomotor control then antisaccades should demonstrate a reliable post-exercise RT reduction, and may exhibit increased response accuracy. In turn, equivalent antisaccade RTs at pre- and post-exercise assessments would indicate that the duration of the single-bout of aerobic exercise used here does not contribute to a reliable improvement to executive function. The present investigation included prosaccades because such actions are mediated via direct retinotopic projections within the superior colliculus (Wurtz & Albano, 1980), and therefore operate largely independent of executive control (Pierrot-Deseilligny, Rivaud, Gaymard, Müri, & Vermersch, 1995). Thus, prosaccades serve as a natural control to antisaccades because they are mediated via subcortical structures that are refractory to exercise-related modulation (see Colcombe & Kramer, 2003). A follow-up experiment (i.e., Experiment 2) involving separate pro- and antisaccade sessions interspersed between a rest interval was included to exclude the possibility that a between-assessment change in antisaccade RTs relate to a practice-related performance benefit.

Experiment 1

Participants completed a 10-minute single-bout of moderate-to-vigorous intensity exercise on a cycle ergometer and I examined pre- and post-exercise pro- and antisaccade performance. As such, Experiment 1 provided a framework to determine whether 10-minutes of aerobic exercise imparts an immediate benefit to executive-related oculomotor control.

Methods

Participants

Fourteen participants (5 female, 9 male; age range = 19-26 years of age) from the University of Western Ontario community volunteered for this research. Participants were right hand dominant (University of Waterloo Handedness Questionnaire), had normal or corrected-tonormal vision, and reported no history of neurological impairment or eye injury. Additionally, participants obtained a full score on the Physical Activity Readiness Questionnaire (PAR-Q) and completed the Godin Leisure-Time Exercise Questionnaire (GLTEQ). The GLTEQ is an objective assessment of typical leisure and physical activity involvement, and is widely used as a screening tool to ensure a normally distributed overall exercise involvement by participants (Godin & Shephard, 1997).

The GLTEQ was used to determine each participant's self-reported weekly frequency for light, moderate, and strenuous activity levels. A score of 23 or less on the questionnaire indicates that an individual partakes in an insufficient amount of weekly physical activity as per the North American Public Health Guidelines (Amireault, Godin, Lacombe, & Sabiston, 2015). All participants in the present study achieved a score of greater than 23 and resulted in a group mean of 75 (SD=45) (**Table 1**). Participants refrained from alcohol and caffeine consumption 12 hours prior to the exercise protocol, did not engage in a severe exercise session 48 hours prior to the protocol, and were encouraged to get eight hours of sleep the night before data collection. All testing sessions took place during the mid-afternoon (i.e., 2 to 4pm). Participants signed consent forms approved by the Office of Research Ethics, University of Western Ontario, and this work was conducted according to the Declaration of Helsinki. Finally, no participant mortality was associated with recruitment.

Table 1. Participant scores on the Godin Leisure Time Exercise Quotient (GLTEQ) for Experiment 1.

^aLight Activity Frequency = Minimal effort e.g., yoga, bowling, golf, easy-walking b Moderate Activity Frequency = Not exhausting e.g., easy bicycling, fast walking, leisure swimming

 $\mathrm{c}V$ igorous Activity Frequency = Rapid heart-beat e.g., running, vigorous swimming, Longdistance bicycling, jogging

 d Note: GLETQ = Godin Leisure Activity Time Quotient;

Leisure Score Index (LSI) Formulation = $(9 \times \text{Vigorous}) + (5 \times \text{Modernate}) + (3 \times \text{Light})$ ^eClassification: LSI \leq 23 = Insufficiently Active; LSI \geq 23 = Active

Exercise Intervention

During the exercise intervention participants sat on a cycle ergometer (Monark 818E Ergometer, Monark Exercise AB, Vansbro, Sweden) with a heart-rate monitor strapped to their chest (Polar Wearlink+ Coded Transmitter, Polar Electro Inc., Lake Success, NY, USA). Participants adjusted the ergometer seat height and handlebar to their individual morphological characteristics and pedaled on the ergometer in the conventional seated position.

The first 2.5 minutes of the intervention included a warm-up at approximately 90W, with the precaution that heart rate did not exceed 50% of their maximum (Karvonen Formulae: see Robergs & Landwehr, 2002). Following the warm-up, participants exercised at a moderate-tovigorous intensity (i.e., 60-85% of predicted maximum heart rate) for 10 minutes. The

moderate-to-vigorous exercise definition used here was based on nomenclature adopted from the Surgeon General's Report on Physical Activity and Health (US Department of Health and Human Services, 1996) and reflects an exercise intensity that promotes cardiorespiratory fitness as well as being sufficient for everyday health. During this timeframe, participants adjusted the resistance lever on the ergometer to maintain the instructed target heart rate level; however, when necessary I prompted the participant to modify the resistance level. Following the 10 minute exercise session participants completed a 2.5-minute cool-down period.

Oculomotor task

Participants sat in front of a tabletop (height 775 mm) during the oculomotor assessment with their head placed in a head/chin rest. A 30-inch LCD monitor (60 Hz, 8 ms response rate, 1,280 x 960 pixels; Dell 3007WFP, Round Rock, TX, USA) located at participants' midline and 550 mm from the front edge of the tabletop was used to present visual stimuli. The gaze location of participants' left eye was measured via a video-based eye-tracking system (Eye-Trac6: Applied Sciences Laboratories, Bedford, MA, USA) sampling at 360 Hz. In addition to the stimulus monitor, two additional monitors visible only to the experimenter provided real-time point of gaze information, trial-by-trial saccade kinematics (e.g. displacement, velocity), and information related to the accuracy of the eye tracking system (i.e., to perform a calibration and recalibration when necessary). Computer events and the presentation of visual stimuli were controlled via MATLAB (7.6: The MathWorks, Natick, MA, USA) and the Psychophysics Toolbox extensions (ver 3.0; Brainard 1997). The lights in the experimental suite were extinguished throughout data collection.

Visual stimuli were presented on a high-contrast black background and included a white fixation cross (1° : 135 cd/cm²) located at the centre of the monitor and target stimuli located at amplitudes 10.5° (i.e., proximal target) and 15.5° (i.e., distal target) left and right of the fixation and in the same horizontal axis. Target stimuli were filled yellow circles (127 cd/cm^2) 2.7° in diameter. At the start of a trial the fixation cross was presented and signaled participants to direct their gaze to its location. Once a stable gaze was attained $(+1.5^{\circ}$ for 420 ms) a randomized foreperiod was initiated (i.e., 1,000 to 2,000 ms). After the foreperiod, the fixation cross was extinguished (i.e., gap paradigm) and a target stimulus was presented 200 ms thereafter. The onset of the target stimulus cued participants to pro- (i.e., saccade to the veridical target location) or antisaccade (i.e., saccade mirror-symmetrical to the target stimulus) "as quickly and accurately as possible". Targets were presented for 50 ms. The brief target presentation was used to preclude extraretinal feedback for pro- and antisaccades (Heath, Weiler, Marriott, & Welsh, 2011).

Pro- and antisaccades were completed in separate and randomly ordered blocks. Within each block, each target location (i.e., left and right of fixation) and target eccentricity (i.e., 10.5° and 15.5°) combination was ordered randomly and presented on 20 trials. Once the pre-exercise oculomotor assessment was completed participants immediately began their single-bout exercise task. Following the single-bout of exercise a second oculomotor assessment (i.e., post-exercise) was completed. The post-exercise assessment was completed from between one and three minutes following the cool-down period (i.e., when an individual participant's heart rate was within 10-15 beats per minute of their resting value). Pre- and post-exercise oculomotor assessments required between 12-15 minutes for completion.

Data Reduction, Dependent Variables and Statistical Analysis

 \overline{a}

Displacement data were filtered offline using a dual-pass Butterworth filter employing a low-pass cut-off frequency of 15 Hz. A five-point central-finite difference algorithm was used to compute instantaneous velocities. Acceleration data were similarly obtained from the velocity data. Saccade onset was determined via velocity and acceleration values that exceeded 30°/s and 8,000 \degree /s², respectively. In turn, saccade offset was determined when velocity fell below 30 \degree /s for 15 consecutive samples (i.e., 42 ms).

Dependent variables were reaction time (RT: time from target onset to saccade onset), the coefficient of variation (CV) of RT (standard deviation/mean x 100%), the percentage of directional errors (i.e., the completion of a prosaccade instead of an instructed antisaccade, and vice versa) and saccade amplitude in the primary (i.e., horizontal) movement direction. Dependent variables were examined via 2 (time: pre-exercise, post-exercise) by 2 (task: prosaccade, antisaccade) by 2 (target eccentricity: 10.5° [proximal target], 15.5° [distal target]) fully repeated measures analysis of variance $(ANOVA)^1$. Trials involving an express saccade

 $¹$ The visual field (i.e., left versus right of fixation) associated with target presentation has been shown to not</sup> reliably influence antisaccade metrics (e.g., West et al. 2009) and for that reason it was not included in the current ANOVA model.

(i.e., $RT < 100$ ms) (Wenban-Smith & Findlay, 1991), an amplitude less than 2° or greater than two standard deviations above a participant- and target-specific mean (Weiler & Heath, 2014), were excluded from data analysis. Less than 5% of trials were removed due the aforementioned criteria.

Results

Reaction time and reaction time variability.

Figure 1 shows percent frequency histograms for pro- and antisaccade RTs at pre- and post-exercise assessments. The panels graphically depict that antisaccade RTs were longer than prosaccades and qualitatively demonstrates the top-down and time-consuming demands of antisaccades. In terms of quantitative analyses, RT produced a main effect for task, $F(1,13) =$ 71.99, $p < 0.001$, $\eta_p^2 = 0.85$, and a time by task interaction, $F(1,13) = 11.49$, $p < 0.01$, $\eta_p^2 = 0.47$. **Figure 2** shows that prosaccade RTs did not reliably vary between pre- and post-exercise assessments (t(13) =0.45, $p = 0.66$, $d_z = 0.17$), whereas antisaccades RTs were shorter for the post- than the pre-exercise assessment $(t(13) = 3.88, p < 0.01, d_z = 1.04)$.

The CV of RT produced main effects of time, $F(1,13) = 11.54$, $p < 0.01$, $\eta_p^2 = 0.47$, and task, $F(1,13) = 48.41$, $p < 0.001$, $\eta_p^2 = 0.79$, and the two variables did not reliably interact, $F(1,13) = 0.28$, $p = 0.60$, $\eta_p^2 = 0.02$. Accordingly, pre-exercise (24, SD=9) and prosaccade (28, SD=9) CV values were larger than their post-exercise (22, SD=10) and antisaccade counterparts $(18, SD=6)$.

Figure 1. Experiment 1: Percent frequency histograms for pro- (top panels) and antisaccade (bottom panels) reaction time (RT: ms) at pre- and post-exercise assessments. The bins for each figure begin at 100 ms and continue to 500 ms with individual bin widths of 20 ms.

Figure 2. Experiments 1 and 2: The large panels show pro- and antisaccade reaction time (RT: ms) for Experiment 1 (top panel) and Experiment 2 (bottom panel) as a function of pre- and postexercise assessments (i.e., Experiment 1) and pre- and post-break assessment (Experiment 2). Error bars represent the 95% within-participants' confidence intervals computed via the meansquared error term for the time by task interaction (Loftus and Masson, 1994). The offset panels in each figure show mean assessment difference scores (Experiment 1: pre-exercise minus postexercise; Experiment 2: pre-break minus post-break) computed separately for pro- and antisaccades. Error bars represent 95% between-participant confidence intervals and the absence of overlap between an error bar and zero (i.e., the horizontal line) can be interpreted as a reliable effect inclusive to a test of the null hypothesis (Cumming, 2013).

Results for directional errors indicated a main effect for task, $F(1,13) = 31.14$, $p < 0.001$, η_p^2 = 0.71, such that antisaccades (11%, SD=9) produced more directional errors than prosaccades (1%, SD=8). As well, and given the objective of this study, **Figure 3** shows that neither the main effect of time, $F(1,13) = 2.41$, $p=0.15$, $\eta_p^2 = 0.16$, nor the time by task interaction, $F(1,13) = 2.81$, $p = 0.12$, $\eta_p^2 = 0.18$, was significant. In other words, the exercise intervention did not reliably modify the percentage of pro- and antisaccade directional errors.

Figure 4 shows the percent frequency histograms for pro- and antisaccade amplitudes and demonstrates that antisaccade amplitudes were shorter than prosaccades – an expected finding attributed to the fact that vector inversion renders motor output specified via a less accurate representation of target location (Heath, Gillen & Weiler, 2015). In terms of quantitative analyses, results yielded a main effect for task, $F(1,13) = 5.70$, $p < 0.05$, $\eta_p^2 = 0.31$, and a task by target eccentricity interaction, $F(1,13) = 46.59$, $p < 0.001$, $\eta_p^2 = 0.78$. **Figure 5** shows that prosaccade amplitudes increased with increasing target eccentricity $(t(13)=11.43, p <$ 0.001, $d_z = 3.15$), whereas antisaccade amplitudes did not (t(13) = 1.05, $p = 0.32$, $d_z = 0.32$). Further, results did not yield a reliable effect of time nor any higher-order interaction involving time, all $F(1,13) < 1.05$, $ps > 0.32$, all $\eta_p^2 < 0.07$.

Figure 3. Experiment 1: Percentage of pro- and antisaccade directional errors (%) at pre- and post-exercise assessments. Error bars represent the 95% within-participants' confidence interval computed via the mean-squared error term for the time by task interaction (Loftus and Masson, 1994).

Exercise Intervention: Experiment 1

Figure 4. Experiment 1: Percent frequency histograms for pro- (top panels) and antisaccade (bottom panels) amplitudes (AMP: \degree) at pre- and post-exercise assessments. The bins for each figure at start at 0° and continue to 30° with individual bin widths of 2° .

Exercise Intervention: Experiment 1

Figure 5. Experiment 1: The large panels in this figure show pro- and antisaccade amplitude (°) as a function of pre- and post-exercise assessment for the proximal (top panel) and distal (bottom panel) targets. Error bars represent the 95% within-participants' confidence interval computed via the mean-squared error term for the time by task interaction (Loftus and Masson, 1994). The offset panels show mean between-assessment difference scores (pre-exercise minus postexercise) computed separately for pro- and antisaccades. Error bars represent 95% betweenparticipant confidence intervals and the absence of overlap between an error bar and zero (i.e., the horizontal line) can be interpreted as a reliable effect inclusive to a test of the null hypothesis (Cumming, 2013).

Experiment 1: Discussion

Antisaccade – but not prosaccade – RTs decreased from the pre- to post-exercise assessment. One interpretation of this finding is that a 10-minute single-bout of moderate-tovigorous intensity aerobic exercise improves executive-related oculomotor control. Alternatively, it is possible that the post-exercise reduction in antisaccade RT relates to a practice effect; that is, from pre- to post-exercise assessments participants were better able to evoke the task-set appropriate for the top-down demands of antisaccades. To address this issue, I recruited a separate corpus of participants for Experiment 2 and included pro- and antisaccade assessments across separate sessions interspersed by a 'break' interval (i.e., participants sat and read a magazine for 15 minutes between pre- and post-break oculomotor assessments).

Experiment 2

Methods

Participants

I recruited twelve participants (6 female, 6 male; age range = 19-26 years of age) for this experiment, and the same inclusion/exclusion criteria and ethics protocol used in Experiment 1 were used here (see **Table 2** for participant-specific GLTEQ values).

Table 2. Participant scores on the Godin Leisure Time Exercise Quotient (GLTEQ) for Experiment 2.

^aLight Activity Frequency = Minimal effort e.g., yoga, bowling, golf, easy-walking b Moderate Activity Frequency = Not exhausting e.g., easy bicycling, fast walking, leisure swimming

 α ^cVigorous Activity Frequency = Rapid heart-beat e.g., running, vigorous swimming, Longdistance bicycling, jogging

 d Note: GLETO = Godin Leisure Activity Time Quotient;

Leisure Score Index (LSI) Formulation = $(9 \times \text{Vigorous}) + (5 \times \text{Modernate}) + (3 \times \text{Light})$ ^eClassification: LSI < 23 = Insufficiently Active; LSI > 23 = Active

Intervention and Oculomotor task

The only difference between Experiment 1 and the present experiment is that I did not employ an exercise intervention; rather, following the initial oculomotor assessment (i.e., prebreak) participants sat and read a magazine for 15 minutes before completing their second oculomotor assessment (i.e., post-break). As such, Experiment 2 was designed to determine whether the post-exercise antisaccade RT benefit observed in Experiment 1 was specific to the aerobic intervention, or is attributed a practice-related performance benefit.

Data Reduction, Dependent Variables and Statistical Analysis

Data post-processing and analyses were the same as Experiment 1. I removed less than 4% of trials from the final data set (see outlier criterion defined in Experiment 1).

Results

Reaction time and reaction time variability.

Figure 6 presents percent frequency histograms for pro- and antisaccade RTs at pre- and post-break intervals. RT produced a main effect for task, $F(1,11) = 57.67$, $p < 0.001$, $\eta_p^2 = 0.84$: RTs for prosaccades (233 ms, $SD = 29$) were shorter than antisaccades (312 ms, $SD = 44$). Further, and given the primary objective of this study, results for RT did not produce a main effect for time or a task by time interaction, all $F(1,11) < 1.01$, $ps > 0.36$, all $\eta_p^2 < 0.03$; that is, neither pro- nor antisaccade RTs decreased from the pre- to post-break assessment (**Figure 2**).

The CV of RT produced main a main effect of task, $F(1,11) = 16.70, p < 0.01, \eta_p^2 = 0.60$, such that prosaccade values $(28, SD=11)$ were larger than antisaccades $(18, SD=8)$. As in Experiment 1, this variable did not elicit a reliable time by task interaction, $F(1,11) = 1.41$, $p =$ 0.30, $\eta_p^2 = 0.11$.

Control: Experiment 2

Figure 6. Experiment 2: Percent frequency histograms for pro- (top panels) and antisaccade (bottom panels) reaction time (RT: ms) at the pre- and post-break assessments. The bins for each figure begin at 100 ms and continue to 500 ms with individual bin widths of 20 ms.

Directional errors and endpoint accuracy.

Antisaccades (14%, SD=28) produced more directional errors than prosaccades (2%, SD=6), $F(1,11) = 6.54$, $p < 0.05$, $\eta_p^2 = 0.37$, and **Figure 7** shows that neither the main effect of time, nor the time by task interaction, all $F(1,11) < 1.90$, $ps > 0.19$; all $\eta_p^2 < 0.01$, were significant.

Figure 7. Experiment 2: Percentage of pro- and antisaccade directional errors (%) at pre- and post-break assessments. Error bars represent the 95% within-participants' confidence interval computed via the mean-squared error term for the task by time interaction (Loftus and Masson, 1994).

Figure 8 shows percent frequency histograms for amplitude. Amplitude produced a main effect for target eccentricity, $F(1,11) = 67.37$, $p < 0.001$, $\eta_p^2 = 0.86$, and an interaction involving task by target eccentricity, $F(1,11) = 114.27$, $p < 0.001$, $\eta_p^2 = 0.91$. Prosaccade amplitudes increased with increasing target eccentricity (t(11) = 19.14, $p < 0.001$, $d_z = 6.89$), whereas antisaccade amplitudes did not reliably vary with target eccentricity (t(11) = 1.44, $p = 0.18$, $d_z =$

involving time, all $F(1,11) < 1.11$, $ps > 0.74$, all $\eta_p^2 = <0.01$.

Control: Experiment 2

0.45) (**Figure 9**). Results did not yield a main effect for time, or any higher-order interaction

Figure 8. Experiment 2: Percent frequency histograms for pro- (top panels) and antisaccade (bottom panels) amplitudes (AMP: \degree) at pre- and post-break assessments. The bins for each figure start at 0° and continue to 30° with individual bin widths of 2° .

Control: Experiment 2

Proximal Target

Figure 9. Experiment 2: The large panels in this figure show pro- and antisaccade amplitude (°) as a function of pre- and post-break assessments for the proximal (top panel) and distal (bottom panel) target eccentricities. Error bars represent the 95% within-participants' confidence interval computed via the mean-squared error term for the time by task interaction (Loftus and Masson, 1994). The offset panels show mean between-assessment difference scores (pre-break minus post-break) computed separately for pro- and antisaccades. Error bars represent 95% betweenparticipant confidence intervals and the absence of overlap between an error bar and zero (i.e., the horizontal line) can be interpreted as a reliable effect inclusive to a test of the null hypothesis (Cumming, 2013).

Between-experiment comparison of GLETQ and Pre-exercise assessment pro- and antisaccade RTs.

GLETO values did not reliably differ between Experiments 1 and 2 (t(24) $<$ 1) – a result demonstrating equivalent between-experiment engagement in leisure time physical activity. As well, I contrasted between-experiment pre-exercise and pre-break pro- and antisaccade RTs via 2 (Experiment: Experiment 1, Experiment 2) by 2 (task: pro-, antisaccade) mixed-groups ANOVA. Results did not elicit reliable main effects or an interaction, all $F < 1$. Thus, participants in Experiments 1 and 2 exhibited comparable baseline oculomotor performance.

Experiment 2: Discussion

Pro- and antisaccade metrics did not reliably vary from the pre- to post-break assessments. As will be outlined in more detail below, such findings support previous work demonstrating that pro- and antisaccade performance remains stable over repeated testing sessions (Klein & Berg, 2001; Roy-Byrne, Radant, Wingerson, & Cowley, 1995), and further evinces that the post-exercise antisaccade RT benefit in Experiment 1 cannot be attributed to a practice-related performance benefit.

General Discussion

Experiment 1 examined whether a 10-minute single-bout of moderate-to-vigorous intensity aerobic exercise differentially influenced pre- and post-exercise pro- and antisaccade control. I included both pro- and antisaccades to determine whether a putative exercise-based change to oculomotor is specific to an executive task. For Experiment 2, I examined the same tasks when completed in separate sessions interspersed by a rest break to determine whether changes in oculomotor control are exercise-specific. In outlining my findings, I will first discuss the general difference between pro- and antisaccade metrics, and subsequently address how aerobic exercise influenced performance for each task.

Pro- and antisaccade RT, directional errors and endpoint accuracy.

Experiments 1 and 2 showed that antisaccade RTs were longer, produced more directional errors and showed decreased amplitude scaling (i.e., reduced accuracy) than prosaccades. This is an expected finding attributed to the fact that antisaccades require the timeconsuming and executive demands of response suppression (i.e., inhibiting a pre-potent prosaccade) and vector inversion (i.e., decoupling the spatial relations between stimulus and response). In particular, the constituent elements of the antisaccade task have been linked to increased activity of: (1) prefrontal executive networks (Everling & Johnston, 2013) that support maintenance of high-level tasks rules and, (2) frontoparietal networks mediating response suppression and vector inversion (Connolly, Goodale, Desouza, Menon, & Vilis, 2000; Ford et al. 2005; for review see Munoz & Everling, 2004). In turn, the more efficient and effective performance of prosaccades relates to the fact that actions with overlapping stimulus and response spatial relations are mediated via direct retinotopic motor maps within the superior colliculus (SC). Thus, the RT findings from the present work indicate that the antisaccade task that I conducted provided a viable tool for examining executive-related oculomotor control.

Pre- and post-exercise pro- and antisaccade performance: Reaction time modulation is selective to executive-related oculomotor control.

Some work has shown that subcortical structures exhibit exercise-based morphological changes. For example, magnetic resonance imaging has shown that higher-fit children (e.g., $VO₂$) max average of 51.5 mL/kg/min) have greater dorsal striatal and hippocampal volumes than their lower fit (e.g., VO_2 max average of 36.4 mL/kg/min) counterparts, and is a result linked to improved performance on memory-based tasks (Chaddock, Erickson, Prakash, Kim, & Voss et al., 2010a; Chaddock, Erickson, Prakash, Vanpatter, & Voss et al., 2010b)². I am, however, unaware of any work reporting that single-bout or chronic exercise programs modulate the activity of midbrain structures (e.g., SC) or influence executive-related functions. Moreover, that prosaccade metrics in Experiment 1 did not reliably vary from the pre- to post-exercise assessment supports the view that a single-bout of exercise does not alter and/or benefit SC activity. In contrast, Experiment 1 showed a 27 ms reduction in antisaccade RTs from the pre- to post-exercise assessment and this result was not associated with concomitant changes in the coefficient of variation of RT, directional errors or endpoint accuracy. The absence of a pre-to-

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 2 Although the hippocampus lies beneath the cerebral cortex it has not been directly identified as a subcortical structure; rather, it is often referred to as being part of the paleocortex (Kandel et al. 2012) or a transition zone between the neo- and allocortex. Regardless, we include the hippocampus here to demonstrate that structures distinct from the neocortex exhibit exercise-related plasticity.

post change in directional errors and endpoint accuracy coupled with the non-selective taskrelated change in the coefficient of variation of RT represent important findings because they demonstrate that the post-exercise RT modulation cannot be tied to a speed-accuracy trade-off (Heath, Samani, Tremblay, & Elliott, 2016a). In other words, participants did not simply decrease their post-intervention antisaccade RTs at the cost of decreased accuracy. Furthermore, in the oculomotor control literature the post-exercise antisaccade RT reduction reported here can only be described as 'large' in magnitude (Munoz & Everling, 2004; DeSimone, Everling, & Heath, 2015) and is an interpretation supported via the large effect size (i.e., $d_z = 1.04$) associated with the comparison of pre- and post-exercise antisaccade RTs (Cohen 1990). Given these findings, a tentative conclusion is that the exercise intervention used here provided a 'boost' to executive-related oculomotor control mechanisms.

An alternate explanation for the post-exercise modulation of antisaccade RTs is that the cognitively challenging nature of the task coupled with its evaluation across temporally proximal assessment (i.e., pre- and post-exercise oculomotor assessments were separated by approximately 15 minutes) allowed participants to develop a refined set of task-rules to improve response suppression and vector inversion. Put another way, a 'practice effect' may account for the improved post-exercise antisaccade RTs. In addressing this issue, it is noted that antisaccade RTs are stable when tested in deliberate practice sessions completed over a 4-week period (Klein & Berg, 2001; Roy-Byrne et al., 1995). Moreover, previous work has shown that within-session antisaccade RTs remain stable even when performed across an extensive (i.e., > 500) number of trials (Gillen & Heath, 2014a; 2014b; Heath et al., 2015; Weiler et al., 2014; 2015). Thus, *indirect* evidence suggests that the change in antisaccade RT observed here cannot be attributed to a practice effect. More directly, Experiment 2 demonstrated that pro- *and* antisaccade RTs (as well as directional errors and accuracy) did not reliably vary when oculomotor assessments were separated by a 15-minute interval that did not include an aerobic task. Accordingly, convergent findings from Experiments 1 and 2 indicate an exercise-specific benefit to the executive-related planning mechanisms supporting antisaccades.

An important issue to address is why the 10-minute exercise duration used here improved executive control, whereas previous work has reported that the benefit is generally limited to durations greater than 20-minutes (Chang et al. 2012; Lambourne & Tomporowski, 2010). One possible explanation is that previous work did not examine executive tasks providing for a

specific measure of executive control. For example, Yagi, Coburn, Estes, and Arruda (1999) had participants perform an oddball identification task (i.e., identify an uncommon shape/sound from familiar shape/sound presentation strings) pre and post a 10-minute single-bout of aerobic exercise (i.e., cycle ergometer at 130-150 beats/min). Similarly, Pontifex and Hillman (2007) had participants complete a single-bout (~12-minute) of aerobic exercise (60% heart rate maximum) and examined pre- and post-exercise performance on a flanker task. Results showed that oddball and flanker tasks did not yield reliable post-exercise improvements in RT or response accuracy. The authors therefore reported that their exercise durations did not provide a sufficient time frame to benefit executive control. It is, however, important to recognize that oddball and flanker tasks entail language-based and visuospatial discrimination that do not provide a *direct* measure of executive control (for detailed list of experiments with exercise durations < 20 minutes see Table 2 of Lambourne & Tomporowski, 2010). A second possible explanation is that previous work employing exercise durations less than 20 minutes were purpose designed to examine cognitive functions apart from executive control. Indeed, studies employing simple/choice RT and perception-based visual discrimination (e.g., Bard & Fleury, 1978; Bender & McGlynn, 1977; McGlynn, Laughlin, & Rowe et al., 1979) reported null postexercise cognitive benefits. In contrast to the above, the antisaccade task employed here is a specific executive task and the increase in antisaccade RTs relative to the prosaccades is overwhelmingly related to response suppression (Olk & Kingstone, 2003; Weiler, Holmes, Mulla, & Heath, 2011) – a processing demand directly tied to executive control (Norman & Shallice, 1986). Moreover, antisaccades are mediated via frontoparietal structures (Ford et al., 2005; Zhang & Barash, 2000; for review see Everling & Johnston, 2013) that show task-specific modulation following single-bout (Hiura, Mizuno, & Fujimoto, 2010; for reviews see Siefert & Secher, 2011; Verburgh et al., 2014) and chronic (Voss et al., 2010) exercise training. I therefore propose that the hands- and language-free nature of antisaccades coupled with the task's reliance on cortical structures sensitive to exercise-based modulations make it an ideal tool for identifying subtle executive changes associated with a brief duration of aerobic exercise (see also Kaufman, Pratt, Levine, & Black, 2012; Heath et al., 2016b; 2017; Peltsch, Hemraj, Garcia, & Munoz, 2014).

Study limitations and future directions.

I recognize that interpretation and extension of my work may be limited to several methodological traits. First, the moderate-to-vigorous intensity exercise intervention used here was predicated on participants maximum predicted heart rate (i.e., Karvonen formulae: HRmax). This measure exhibits considerable between-participant variability and is dependent on individual lifestyle characteristics (i.e., body weight, level of physical fitness) (Whaley, Kaminsky, Dwyer, Getchell, & Norton, 1992). The HRmax may have therefore provided a limited basis for ensuring comparable between-participant exercise intensity and aerobic output. Future work should employ a more quantitative determinant of exercise intensity (i.e., participant-specific $VO₂max$ or lactate threshold values) to identify the intensity level benefiting executive control following a short-duration exercise session. Second, the participants used in this study were young and reported a healthy lifestyle as determined via the GLTEQ. It is therefore unclear whether the exercise intervention used here would serve to produce an executive 'boost' for individuals outside the current age range, individuals who do not partake in a physically active lifestyle, and individuals in the prodromal stages of Alzheimer's disease (i.e., mild cognitive impairment (MCI), cognitive impairment not dementia (CIND)). An important research question is represented here, given previous work showing that chronic (i.e., 6-month) aerobic and/or resistance training programs improve executive-related oculomotor control in the MCI and CIND populations (Heath et al. 2016b; 2017). It may be that individuals from the above-mentioned groups who are unable to commit to chronic exercise programs or are physically limited to short-duration exercise sessions may accrue an executive benefit from the 10-minute single-bout protocol used here. Third, it is unclear how long the executive benefit persists post-exercise. In the present study, the post-exercise oculomotor assessment was completed within 18 minutes of the exercise intervention (see *Methods: Oculomotor Task*). Chang et al's (2012) meta-analysis reported that for exercise durations of 20 minutes or greater the largest positive effect on executive control was observed when executive performance was examined 11-20 minutes post-exercise (i.e., the time frame used here), whereas longer postexercise delays (>20 minutes) produced smaller to negligible effects. It would therefore be interesting to employ the antisaccade task across a range of post-exercise intervals to identify the time frame by which executive performance benefits persist. Additionally, subsequent work should employ shorter intervals (<10 minutes) as the minimum time frame for the antisaccade

benefit, which would further our knowledge to the extent that an aerobic exercise intervention could serve to produce this executive 'boost'.

Conclusions

The present findings demonstrate that a 10-minute single-bout of aerobic exercise at a moderateto-vigorous intensity improved antisaccade – but not prosaccade – planning times. I believe that such results add importantly to the literature insomuch as they demonstrate that the antisaccade task provides a reliable basis to detect subtle improvements to executive control for exercise durations as brief as 10 minutes.

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Appendix A

Approval Notice from the Office of Research Ethics, The University of Western Ontario.

Research Ethics Western Research
Research Western University Health Science Research Ethics Board
HSREB Delegated Initial Approval Notice **HSREB** Delegated Initial Approval Notice

Principal Investigator: Dr. Matthew Heath
Department & Institution: Health Sciences\Kinesiology, Western University Review Type: Full Board

Review Type: rull Board

HSREB File Number: 107560

Study Title: The Effects of Exercise on Cognitive Abilities Using Saccades

Snonsor: Natural Sciences and Engineering Bonarch Council Sponsor: Natural Sciences and Engineering Research Council

HSREB Initial Approval Date: February 17, 2016
HSREB Expiry Date: February 17, 2017

Documents Approved and/or Received for Information:

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above named study, as of the HSREB Initial Approval Date noted above.

HSREB approval for this study remains valid until the HSREB Expiry Date noted above, conditional to timely submission and acceptance of HSREB Continuing Ethics Review.

The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice Practices (ICH E6 R1), the Ontario Personal Health Information Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Appendix B

Continuing Approval Notice from the Office of Research Ethics, The University of Western Ontario.

Curriculum Vitae

