

---

Electronic Thesis and Dissertation Repository

---

4-3-2020 10:00 AM

## Oculomotor Task-Switching Performance Improves and Persists Following a Single Bout of Aerobic Exercise

Diksha Shukla  
*The University of Western Ontario*

Supervisor  
Heath, Matthew  
*The University of Western Ontario*

Graduate Program in Kinesiology

A thesis submitted in partial fulfillment of the requirements for the degree in Master of Science  
© Diksha Shukla 2020

Follow this and additional works at: <https://ir.lib.uwo.ca/etd>



Part of the [Cognitive Neuroscience Commons](#), [Exercise Science Commons](#), and the [Motor Control Commons](#)

---

### Recommended Citation

Shukla, Diksha, "Oculomotor Task-Switching Performance Improves and Persists Following a Single Bout of Aerobic Exercise" (2020). *Electronic Thesis and Dissertation Repository*. 6905.  
<https://ir.lib.uwo.ca/etd/6905>

This Dissertation/Thesis is brought to you for free and open access by Scholarship@Western. It has been accepted for inclusion in Electronic Thesis and Dissertation Repository by an authorized administrator of Scholarship@Western. For more information, please contact [wlsadmin@uwo.ca](mailto:wlsadmin@uwo.ca).

# Abstract

Executive function includes the core components of response inhibition, working memory, and cognitive flexibility. Interestingly, an accumulating evidence has reported that inhibitory control and working memory improve following a single bout of exercise. It is, however, largely unclear whether cognitive flexibility elicits a similar post-exercise benefit. Accordingly, Chapter Two of my thesis examined whether 20-min of aerobic exercise provides an immediate post-exercise ‘boost’ to cognitive flexibility. Chapter Three examined for how long a putative post-exercise benefit persists. Cognitive flexibility was examined via an AABB task-switching paradigm wherein participants alternated between a well-practiced and a novel oculomotor task pre- and post-exercise. Chapter Two showed an immediate post-exercise benefit to cognitive flexibility and Chapter Three demonstrated that the benefit persists for up to 47-min post exercise. As such, my thesis provides convergent evidence that a single bout of exercise benefits each core component of executive function.

## **Keywords**

Executive function

Task-switching

Oculomotor

Single bout

Saccades

Switch-cost

## Summary for Lay Audience

An accumulating literature indicates an overall positive effect of acute exercise on executive function. Executive function is essential to activities of daily living and includes the core components of inhibitory control, working memory and cognitive flexibility. Notably, the majority of research demonstrating that exercise provides a ‘boost’ to executive function has focused on inhibitory control and working memory tasks. It is therefore largely unclear whether exercise similarly benefits cognitive flexibility. To address this issue, I used a ‘task-switching’ paradigm wherein participants alternated – or ‘switched’ – between different oculomotor (i.e., eye movement) tasks after every second trial prior to and after a 20-min single bout of aerobic exercise. In my first experiment, a single bout of aerobic exercise provided an immediate post-exercise improvement to cognitive flexibility. In a subsequent experiment, I showed that the benefit persisted for up to 47-min post-exercise. Accordingly, my results provide direct evidence that exercise improves cognitive flexibility and lends to convergent support for the view that an exercise benefit extends to each core component of executive function.

## Co-Authorship Statement

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, recruited participants, collected, analyzed and interpreted data, and prepared the manuscripts. I received support from an undergraduate research assistant (Zain Al-Shamil) in recruiting participants and collection of data for Chapter Two. For this manuscript, Diksha Shukla was the first author, and Zain-Al Shamil, Dr. Glen Belfry, and Dr. Matthew Heath served as co-authors in the published version (under review) of the work.

## Acknowledgements

First and foremost, I would like to acknowledge and thank my graduate supervisor, Dr. Matthew Heath for taking me on as a student and providing me with many valuable learning opportunities. Thank you for being so patient during troubleshooting and pushing me to think critically about our work. I greatly appreciate the time that you have dedicated to helping me improve my skills to succeed as a researcher. Your constant support and guidance for my future endeavours is truly valued and appreciated.

I would like to thank all my participants for their patience and generosity. Without their commitment, these studies would not have been possible. Also, I would like to thank my lab mates and friends. I consider myself very lucky to have met such fun, intelligent and inspiring people. Thank you for your constant support, guidance, and feedback that you have provided over the two years. I will forever cherish our endless laughs and great memories.

To my family and loved ones, thanks for always being so supportive and encouraging. Without you, none of this would have been possible.

# Table of Contents

Abstract.....	ii
Summary for Lay Audience.....	iii
Co-Authorship Statement.....	iv
Acknowledgements.....	v
Table of Contents.....	vi
List of Figures.....	viii
List of Appendices.....	xi
Chapter 1.....	1
1 Literature Review.....	2
1.1 Executive function.....	2
1.2 Aerobic exercise and executive function.....	5
1.3 Proposed mechanisms associated with the exercise-based improvement to executive function.....	7
1.4 Oculomotor task-switching.....	8
1.5 References.....	10
Chapter 2.....	16
2.1 Introduction.....	17
2.2 Methods.....	20
2.2.1 Experiment 1.....	20
2.2.2 Experiment 2.....	25
2.3 Results.....	26
2.3.1 Experiment 1.....	26
2.3.2 Experiment 2.....	29
2.4 Discussion.....	32

2.5	Conclusions.....	35
2.6	References.....	36
Chapter 3	.....	42
3.1	Introduction.....	43
3.2	Methods.....	46
3.3	Results.....	50
3.4	Discussion.....	56
3.5	Conclusions.....	58
3.6	References.....	59
Chapter 4	.....	59
Appendices	.....	65

# List of Figures

**Figure 1.** Lateral view of the three regions of the prefrontal cortex (i.e., dorsolateral prefrontal cortex, orbitofrontal cortex and anterior cingulate cortex) associated with executive function. Reproduced from Zelazo, Blair, & Willoughby (2016). National Center for Education Research. 11..... 3

**Figure 2.** Schematic of visual events across five successive trials. Participants alternated between pro- and antisaccades after every second trial (i.e., AABB). In this schematic, the green fixation cross denotes a saccade to the target’s veridical location (i.e., prosaccade), whereas the red fixation cross cued a saccade to the target’s mirror-symmetrical (i.e., antisaccade) location. For usability the schematic depicts only a single target eccentricity presented to the right of fixation; however, in the current investigation the target eccentricity (i.e., 13.5° and 17.5°) and target location (i.e., left and right of fixation) were pseudo-randomized. .... 23

**Figure 3.** The main panels show pro- and antisaccade reaction time (ms) percent frequency histograms at pre- (top panels) and post-exercise (bottom panels) assessments for task-switch and task-repeat trials (bin widths of 50 ms). The inset left panel (A) shows group mean pro- and antisaccade task-switch and task-repeat reaction times (ms) at pre- and post-exercise assessments. Error bars represent 95% within-participant confidence intervals computed via the mean-squared error term for the task by task-transition interaction (Loftus & Masson, 1994). The inset right panel (B) shows group mean pro- and antisaccade reaction time difference scores (i.e., task-switch minus task-repeat) at pre- and post-exercise assessments. Error bars represent 95% between-participant confidence intervals. The absence of overlap between an error bar and zero (i.e., the horizontal line) represents a reliable effect inclusive to a test of the null hypothesis (Cumming, 2013). .... 27

**Figure 4.** The main panels show pro- and antisaccade saccade amplitude percent frequency histograms at pre- (top panels) and post-exercise (bottom panels) assessments for task-switch and task-repeat trials to the proximal (i.e., 13.5°) and distal (i.e., 17.5°) targets eccentricities (bin widths of 2°). The vertical solid and dashed lines represent veridical locations for proximal and



distal targets, respectively. The figure provides a qualitative demonstration that amplitudes for prosaccades – but not antisaccades – increased in relation to target eccentricity. .... 29

**Figure 5.** The left panels depict group mean reaction time (A), movement time (B), saccade amplitude (C) and saccade amplitude variability (D) for pro- and antisaccade task-switch and task-repeat trials at pre- and post-break assessments. Error bars represent 95% within-participant confidence intervals. The right panels show pro- and antisaccade reaction time (A), movement time (B), saccade amplitude (C) and saccade amplitude variability (D) difference scores (task-switch minus task-repeat) at pre- and post-break assessments. Error bars represent 95% between-participant difference scores..... 31

**Figure 6.** Panel A provides a schematic of visual event for stimulus-driven and minimally delayed saccades. The green fixation cross cued a saccade immediately to a target’s veridical location (i.e., stimulus-driven prosaccade), whereas the red fixation cross cued a saccade at target offset (i.e., minimally delayed prosaccade). Notably, the schematics shows only a single target eccentricity to the right of fixation; however, in the task-switching block the target eccentricity (i.e., 13.5° and 17.5°) and target location (i.e., left and right of fixation) were pseudo-randomized. Panel B shows the timeline of four oculomotor assessments including pre-exercise (Pre-), immediate (Imme.), 30-, and 60-min post-exercise assessments in relation to the timing of the exercise protocol. .... 49

**Figure 7.** Exemplar participant’s trial-to-trial position by time trajectories for stimulus-driven and minimally delayed task-switch and task-repeat saccades at pre-, immediate, 30- and 60-min post-exercise assessments. (Note: time zero represents response cuing). For simplicity, task-switch and task-repeat saccades are depicted as negative and positive trajectory deflections, respectively. .... 52

**Figure 8.** The main panels show reaction time (ms) percent frequency histograms for stimulus-driven and minimally delayed task-switch and task-repeat saccades at pre- and immediate, 30-, and 60-min post-exercise with bin widths of 50 ms. The light and dark grey rectangles in each

panel denote anticipatory (<100 ms) and short-latency (100 to <200 ms) responses, respectively.  
..... 53

**Figure 9.** The left panel (A) shows group mean stimulus-driven (SD) and minimally delayed (MD) task-switch and task-repeat saccade reaction times (ms) at pre- and each post-exercise assessment. Error bars represent 95% within-participant confidence intervals computed via the mean-squared error term for time by task by task-transition interaction (Loftus & Masson, 1994). The right panel (B) shows group mean SD and MD saccade reaction time difference scores (i.e., task-switch minus task-repeat) at for each assessment. Error bars represent 95% between-participant confidence intervals and the absence of overlap between an error bar and zero (i.e., the horizontal line) represents a reliable effect inclusive to a test of the null hypothesis (Cumming, 2013). ..... 54

**Figure 10.** The main panels show saccade gain (i.e., saccade amplitude/veridical target location) percent frequency histograms for stimulus-driven (left panels) and minimally delayed (right panels) task-switch and task-repeat saccades at each time of assessment (bin width= 0.1). The textbox within each panel contains the mean and standard deviation for proximal (i.e., 13.5°) and distal (i.e., 17.5°) targets. .... 55

## List of Appendices

Appendix A: Approval notice from the Office of Research Ethics, The University of Western Ontario.....	65
Appendix A: Approval notice from the Office of Research Ethics, The University of Western Ontario.....	66

# Chapter 1

## General Introduction

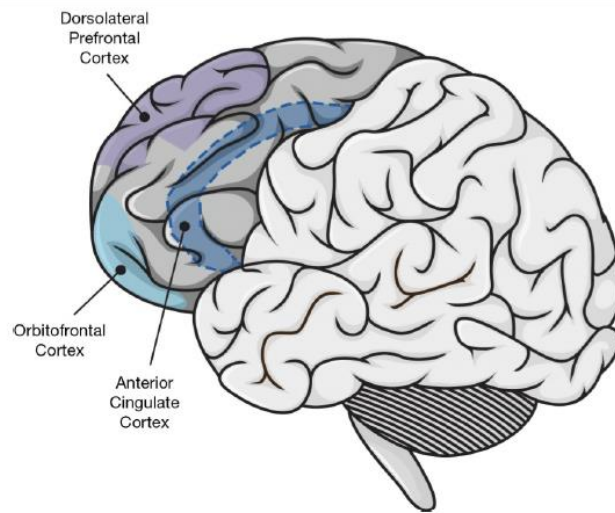
# 1 Literature Review

The goal of my thesis was to determine whether a single bout of moderate-to-heavy intensity aerobic exercise improves the cognitive flexibility core component of executive function. In addition, I sought to determine for how long a putative improvement to cognitive flexibility persists post-exercise. In developing my thesis document, I first provide a general review of: 1) executive function, 2) exercise-based improvements to executive function, 3) the proposed neurobiological mechanisms for a post-exercise executive benefit, and 4) a general outline of the oculomotor task-switching literature.

## 1.1 Executive function

Executive function refers to the top-down cognitive processes that play an essential role in our ability to adapt to a dynamic environment. For example, imagine that our brain is analogous to a control tower at an airport. Flight patterns and ground communication all depend on the control tower's ability to process the flow of information, pay attention to and remember instructions, and attend to multiple tasks to avoid an accident. Indeed, our brain similarly exercises executive function to effectively implement attentional- and motor-related goals. The three core components underlying executive function include: (1) inhibitory control, (2) working memory, (3) and cognitive flexibility (Diamond, 2013). Convergent evidence from neuroimaging and lesion studies have demonstrated that executive function is primarily mediated via extensive prefrontal cortex (PFC) circuitry. The three regions of PFC that are particularly relevant to executive function include: (1) dorsolateral prefrontal cortex (DLPFC), (2) orbitofrontal cortex (OFC), and (3) anterior cingulate cortex (ACC) (Royall et al., 2002) (see **Figure 1**). The DLPFC is responsible for mediating higher-order functions including planning, sequencing, goal setting, inhibitory control, working memory, set shifting, self-monitoring, and self-awareness (Diamond, 2013). In contrast, the OFC is responsible for initiating social and internally driven behaviours, and inhibiting inappropriate behavioural responses (Truelle, Le Gall, Joseph, & Aubin, 1995). Finally, the ACC plays a role in monitoring behaviour and behaviour correction (Mansouri, Buckley, Fehring, & Tanaka, 2019). In my literature review, I will discuss the role that the DLPFC plays in executive-mediated tasks (e.g., inhibitory control and working memory tasks) and further investigate its involvement in cognitive flexibility. The

below review will emphasize the role of behavioural tasks in assessing intact and impaired executive function.



**Figure 1.** Lateral view of the three regions of the prefrontal cortex (i.e., dorsolateral prefrontal cortex, orbitofrontal cortex and anterior cingulate cortex) associated with executive function. Reproduced from Zelazo, Blair, & Willoughby (2016). National Center for Education Research. 11.

A common executive function task used to examine inhibitory control is the Stroop Interference Task (Stroop, 1935). A classic Stroop Interference task involves a series of words printed in ink congruent (i.e., the word **RED** printed in red ink) or incongruent (i.e., the word **RED** printed in green ink) to the word meaning. It has been consistently shown that naming the colour of an incongruent condition (i.e., non-standard colour-naming task) results in longer reaction times (or response times) and more naming errors than the congruent word/colour mapping condition (i.e., standard word-naming task) (for review see MacLeod, 1992). The “Stroop Interference Effect” proposes that non-standard colour-naming is a controlled process dependent on the allocation of attention to one stimulus and inhibition of the other dominant stimulus, whereas standard word-naming is an automatic process that requires minimal top-down control. Furthermore, lesion and neuroimaging studies have demonstrated the role of the DLPFC in supporting appropriate response inhibition in the Stroop Interference task. For example, Stuss and colleagues (Stuss, Floden, Alexander, Levine, & Katz, 2001) recruited 51 patients with single focal brain lesions to frontal (e.g., PFC) and non-frontal regions, as well as 26 healthy controls and had them perform the Stroop Interference task. Results showed patients with frontal

lesions elicited longer reaction times (RTs) and increased response errors compared to patients with lesions in non-frontal regions or the healthy control group; that is, frontal patients exhibited a larger interference effect. Moreover, MacDonald and colleagues' (MacDonald, Cohen, Stenger, & Carter, 2000) functional magnetic resonance imaging (fMRI) study employed a Stroop Interference task in an AABB task-switching paradigm (see details below) and demonstrated that the DLPFC was selectively active during the preparatory cue period for non-standard colour-naming task as compared with standard word-naming task and this activity was correlated with reduced Stroop Interference Effects. Accordingly, these findings support the assertion that the DLPFC supports the inhibitory control component of executive function.

The n-back task (Kirchner, 1958) has been used to examine the working memory component of executive function. In the n-back task, a series of visual stimuli are presented, and participants are asked whether a current stimulus matches a stimulus n trials before. The n-back task therefore requires the top-down control of maintaining the appropriate task goal in working memory (Gajewski, Hanisch, Falkenstein, Thönes, & Wascher, 2018). The association between performance on the n-back task (i.e., 1, 2, and 3 n-back task) and executive function is supported by a fMRI-based meta-analyses demonstrating that the PFC elicits increased activity as a function of n-back task complexity (Owen, McMillan, Laird, & Bullmore, 2005). Further, León-Domínguez and colleagues (León-Domínguez, Martín-Rodríguez, & León-Carrión, 2015) examined PFC activity using functional near-infrared spectroscopy (fNIRS) and showed increased blood flow to this area during n-back task performance – a result indicating a functional hyperemia to support increased neural demands during n-back performance.

The third component of executive function is cognitive flexibility and is a process Diamond (2013) referred to as set-shifting and representing "...being flexible enough to adjust to changed demands or priorities" (p. 149). This component is most often investigated using a task-switching paradigm wherein participants alternate between different tasks in an AABB paradigm. Task-switching paradigms include two trial-types: a trial in which a task is preceded by its same task counterpart (i.e., task-repetition trial) and a trial preceded by a different task (i.e., task-switch trial). The literature has consistently reported that task-switch trials have longer RTs than task-repetition trials – a result referred to as a *switch-cost* (see Kiesel et al., 2010 for review). Moreover, it has been shown that the executive demands of a task can asymmetrically influence a switch-cost. In a classic demonstration of this, Allport, Styles, & Hsieh (1994) had

participants alternate between word- (i.e., standard task) and colour-naming (i.e., non-standard task) variants of the Stroop task every second trial (i.e., AABB) and reported that a colour- to word-naming switch (i.e., task-switch trial) increased reaction time (RT), whereas the converse switch did not influence performance (Allport et al., 1994). In turn, RT did not reliably differ when word- and colour-naming tasks were preceded by their same task-type (i.e., task-repeat trial). The authors proposed that the non-standard stimulus-response (SR) mapping of colour-naming engenders an executive task-set that persists inertially and proactively interferes with a subsequent standard response (i.e., task-set inertia hypothesis). As well, the task-set inertia hypothesis contends that alternating from a standard to a non-standard response does not produce a ‘switch-cost’ because the former is planned independent of an executive task-set (for review see Monsell, 2003; see also Wylie & Allport, 2000). In support of the hypothesis, neuroimaging studies have shown an increased signal change in frontal executive regions for task-switch compared to task-repeat trials – a result taken to reflect the persistent activation of a non-standard task-set (for meta-analysis see Derrfuss, Brass, Neumann, & von Cramon, 2005).

## 1.2 Aerobic exercise and executive function

It is well-known that long-term aerobic and/or resistance training programs improve executive function (for review see, Colcombe & Kramer, 2003). For example, Padilla and colleagues (2013) examined whether chronic aerobic exercise in young adults is associated with improved RT in a stop-signal task (SST) (Padilla, Perez, Andres, & Parmentier, 2013). Notably, the SST entails “go” trials requiring a pre-potent response to a stimulus, and “stop” trials wherein participants are required to successfully withhold their response (i.e., a measure of inhibitory control). Padilla et al. reported that regular exercisers (i.e., individuals exercising for minimum of 3 days a week for at least 10 years) produced shorter SST RTs than a group who had not exercised for more than 2 hrs per week over the last 4 years. Furthermore, a follow up study by Padilla, Pérez, & Andrés (2014) examined whether young healthy regular exercisers exhibited higher working memory and inhibitory capacities compared to a sedentary group. Results indicated that regular exercisers simultaneously managed two verbal tasks (i.e., working memory) and produced shorter SST RTs (i.e., inhibitory control) than sedentary individuals. In turn, a randomized control study investigated the effect of 6 months of aerobic exercise (i.e., brisk walking) or strength and flexibility training (i.e., toning and stretching) on cognitive



flexibility in healthy older adults (Kramer et al., 2001). Cognitive flexibility was examined via a paradigm wherein trials were alternated between odd/even (i.e. parity) and vowel/consonant judgement tasks. Results showed that the switch-cost magnitude for the brisk walking group decreased over the course of the 6 months aerobic exercise, whereas no such benefit was observed for the stretching and toning group. Furthermore, Hillman and colleagues (2006) investigated cognitive flexibility in young and older regular exercisers and non-exercisers via a parity and size judgement task-switching paradigm (Hillman, Kramer, Belopolsky, & Smith, 2006). Notably, the authors reported that the amplitude of the P300 event-related brain potential (ERP) was larger for regular exercisers than their non-exercise counterparts – a result interpreted to reflect that physically active individuals have improved task-switching efficiency (see also Themanson, Hillman, & Curtin, 2006). Thus, convergent evidence demonstrates that regular exercisers (as well as those that participated in chronic interventions) exhibit improved performance in each core component of executive function (Colcombe et al., 2004).

In addition to chronic exercise, it is important to recognize that a single bout of exercise can provide a ‘boost’ to executive function (for meta analyses see Chang, Labban, Gapin, & Etnier, 2012; Lambourne & Tomporowski, 2010; Ludyga, Gerber, Brand, Holsboer-Trachsler, & Pühse, 2016). For example, Li et al. (2014) employed the n-back task and concurrent fMRI pre- and post- 20-min of aerobic exercise (via cycle ergometer at 60-70% of estimated maximal heart rate:  $HR_{max}$ ) and showed improved post-exercise performance that was linked to greater task-based activity within PFC networks. In turn, Chang et al. (2014) employed the Stroop Interference task pre- and post- 20-min of aerobic exercise (via cycle ergometer at 65%  $VO_{2max}$ ) and reported a reduced Stroop Interference Effect post-exercise. Similarly, Yanagisawa et al. (2010) reported shorter RTs in Stroop Interference task following acute aerobic exercise at moderate intensity (50%  $VO_{2peak}$ ) and showed that this performance benefit was linked to increased task-based activity within the PFC.

A limitation of the single-bout exercise literature is that the majority of the work has focused on inhibitory control and/or working memory tasks (for review see Table 1 of Ludyga et al., 2016). To my knowledge, however, only three studies have examined whether a single bout of exercise positively benefits cognitive flexibility and the results of this work are mixed. For example, Tsai and colleagues (2016) employed an AABB paradigm involving parity and size judgment tasks to assess whether 30-min of aerobic exercise (via treadmill at 60% of  $VO_{2max}$ )

improves task-switching in young adults classified as high-fit ( $VO_{2max} > 49.2$  ml/kg/min) and low fit ( $VO_{2max} < 43.1$  ml/kg/min) (Tsai, Pan, Chen, Wang, & Chou, 2016). The authors reported a 58 ms reduction in the switch-cost magnitude for the high-fit group; however, no such benefit was observed for low-fit individuals. In contrast, Tomporowski and Ganio (2006) asked ‘recreationally active’ healthy young adults to switch between parity and vowel/consonant judgement tasks in an ABB paradigm following a 40-min bout of aerobic exercise (via cycle ergometer at 60%  $VO_{2max}$ ). The results indicated that exercise did not influence task-switching efficiency and the authors concluded that task-switching paradigms do not provide the requisite resolution to detect post-exercise benefits to cognitive flexibility. Furthermore, Bae and Masaki (2019) had healthy young adults complete a 30-min acute bout of exercise (via treadmill at 70% of  $HR_{max}$ ) and examine pre- and post-exercise cognitive flexibility via a parity and size judgment task (cf. Tsai et al., 2016). Results showed shorter RTs for task-switch trials – a result suggesting improved post-exercise task-switching efficiency.

### 1.3 Proposed mechanisms associated with the exercise-based improvement to executive function

The chronic exercise literature has found that regular exercisers and those who commit to a long-term (>6 months) exercise intervention demonstrate increased hippocampal neuronal density – a region supporting learning and memory (van Praag, 2008). Accordingly, neurogenesis and cell proliferation have been implicated as a primary mechanism for improved executive function following chronic exercise (Clark et al., 2008; Lemaire, Koehl, Le Moal, & Abrous, 2000). In terms of a single bout of exercise, the mechanism is likely different given the functional timeframe for neurogenesis in the adult brain (Ming & Song, 2011). Thus, several other neurobiological mechanisms have been linked to the post-exercise executive benefit. One view holds that transient neurochemical changes such as an increase in serum brain-derived neurotrophic factor (BDNF) improves executive function following a single bout of exercise (for review, see Knaepen, Goekint, Heyman, & Meeusen, 2010). For example, Hwang et al. (2016) assessed the effect of 20-min of acute exercise (via treadmill at 85-90%  $VO_{2max}$ ) on Stroop Interference task performance and concurrently measured serum BDNF pre- and post-exercise. The authors reported improved Stroop Interference task RTs which were positively correlated with an increase in BDNF concentration. Another possible mechanism is an exercise-based

increase in catecholamine (e.g., dopamine, norepinephrine: DA, NE) concentration that improves physiological and psychological arousal – a parsimonious proposal given that frontoparietal regions are regulated by DA and NE (Hershey et al., 2004). A meta-analysis by McMorris, Sproule, Turner, & Hale (2011) reported that acute aerobic exercise at an intermediate intensity (~ 50-75%  $VO_{2max}$ ) improved working memory performance and was associated with an increase in DA and NE metabolites. These findings indirectly suggest that the increase in BDNF and catecholamine concentration associated with a single bout of exercise improves executive function. Another candidate mechanism is increased cerebral blood flow (CBF). Indeed, it is well known that exercise produces an increase in CBF and that increased executive demands result in an increase in functional hyperaemia (Moore & Cao, 2008; Ogoh & Ainslie, 2009). For example, Byun et al. (2014) used fNIRS to show that enhanced cortical hemodynamic changes in the PFC following a 10-min bout of aerobic exercise (via cycle ergometer at 30%  $VO_{2peak}$ ) coincided with improved inhibitory control (i.e., Stroop task). Indeed, it is possible that the mechanical- and temperature-based changes associated with increased CBF improves neural efficiency in the PFC circuitry supporting executive function (i.e., the hemo-neural hypothesis; see Moore & Cao, 2008).

## 1.4 Oculomotor task-switching

My thesis work seeks to determine whether a single bout of exercise improves cognitive flexibility. In pursuing this objective, I employed an oculomotor task-switching paradigm previously developed by my lab group (Tari, Fadel, & Heath, 2019; Tari & Heath, 2019; Weiler, Hassall, Krigolson, & Heath, 2015; Weiler & Heath, 2012a, 2012b, 2014a, 2014b; Weiler, Mitchell, & Heath, 2014). The rationale for employing an oculomotor task-switching paradigm is that previous work may not have observed a reliable post-exercise benefit to cognitive flexibility due to the inclusion of tasks involving non-executive processes such as language, numerosity and parity judgements (see Bae & Masaki, 2019; Tomporowski & Ganio, 2006; Tsai et al., 2016). This represents a salient limitation of previous studies because the aforementioned cognitive processes do not benefit from a single bout of exercise (Chang et al., 2012). As such, one of the oculomotor task-switching paradigm developed by my group involves pro- and antisaccades arranged in an AABB paradigm. Prosaccades are standard oculomotor task (i.e., direct overlap between stimulus and response [SR] spatial relations) requiring a saccade to a

veridical target and are mediated via direct retinotopically organized maps within the superior colliculus (SC) (Wurtz & Albano, 1980). Prosaccades therefore operate largely independent of executive control (Pierrot-Deseilligny, Rivaud, Gaymard, Müri, & Vermersch, 1995). In contrast, antisaccades are non-standard and executive-mediated task requiring the decoupling of SR spatial relations and the evocation of a saccade to a target's mirror-symmetrical location. Convergent studies have shown that antisaccades produce longer RTs (Hallett, 1978), more directional errors (Fischer & Weber, 1992) and less accurate and more variable endpoints than prosaccades (Dafoe, Armstrong, & Munoz, 2007; Gillen & Heath, 2014). The behavioural 'costs' of antisaccades have been attributed the executive demands of a suppressing a pre-potent prosaccade (i.e., response suppression) and the visual remapping (i.e., 180° spatial transformation) of a target's coordinates (i.e., vector inversion) (for review see Munoz & Everling, 2004). Moreover, neuroimaging and lesion studies have shown that the performance of a directionally correct antisaccade is contingent upon increased activity within the PFC (for review see Munoz & Everling, 2004). Notably, work by my group has shown that pro- and antisaccades performed in an AABB paradigm elicit a *unidirectional prosaccade switch-cost* (Weiler et al., 2014, 2015; Weiler & Heath, 2012a, 2012b, 2014a, 2014b). More specifically, a prosaccade preceded by an antisaccade (i.e., task-switch prosaccade) produces longer RTs compared to when a prosaccade is preceded by its same task-type (i.e., task-repeat prosaccade). In turn, antisaccades RTs do not reliably vary across task-switch and task-repeat trials. In accounting for these results, my group has drawn upon Allport et al.'s (1994) task-set inertia hypothesis and the contention that the evocation of an antisaccade requires an executive mediated task-set that proactively delays the planning of a subsequent prosaccade. In support of this view, results from an event-related brain potential (ERP) study by my group showed that task-switch prosaccades produce a P300 amplitude comparable to task-switch and task-repeat antisaccade which is distinct from that of task-repeat prosaccades (Weiler et al., 2015).

In two most recent studies, my group sought to determine whether the unidirectional prosaccade switch-cost is related to the executive demands of response suppression and/or vector inversion (Tari et al., 2019; Tari & Heath, 2019). To address this issue, Tari et al. employed an AABB paradigm using the same stimulus-driven (SD) (pro)saccades (i.e., saccade at target onset) as used in my group's earlier task-switching work (e.g., Weiler & Heath, 2015). Notably, however, SD saccades were alternated with minimally delayed (MD) (pro)saccades (i.e., saccade

at target offset). MD saccades require participants to withhold their response at target onset and saccade in the target's veridical location only *after* the target is extinguished. Accordingly, MD saccades require response suppression without the vector inversion demands required for antisaccades. Results revealed that SD task-switch saccades produced RTs that were 25-30 ms longer than their task-repeat counterparts, whereas RTs for MD task-switch and task-repeat saccades did not reliably differ (see also Tari & Heath, 2019). This finding shows that an oculomotor switch-cost is directly attributed to the executive demands of response suppression. Moreover, I wish to emphasize that the magnitude of the switch-cost observed for the SD and MD task-switching paradigm is greater than a pro- and antisaccade task-switching paradigm. This is important because Davranche and Audiffren (2004) stated that a robust magnitude difference must be observed between tasks when examining post-exercise changes in executive function.

## 1.5 References

- Allport, A., Styles, E.A., & Hsieh, S. (1994). *Shifting intentional set: exploring the dynamic control of tasks*, in: Umiltà, C., Moscovitch, M., (Eds.), *Attention and Performance XV*. MIT Press., Cambridge, pp. 421-452.
- Bae, S., & Masaki, H. (2019). Effects of acute aerobic exercise on cognitive flexibility required during task-switching paradigm. *Frontiers in Human Neuroscience*, *13*, 260.
- Byun, K., Hyodo, K., Suwabe, K., Ochi, G., Sakairi, Y., Kato, M., ... & Soya, H. (2014). Positive effect of acute mild exercise on executive function via arousal-related prefrontal activations: an fNIRS study. *Neuroimage*, *98*, 336-345.
- Chang, Y.K., Chi, L., Etnier, J.L., Wang, C.C., Chu, C.H., & Zhou, C. (2014). Effect of acute aerobic exercise on cognitive performance: Role of cardiovascular fitness. *Psychology of Sport and Exercise*, *15*, 464-470.
- 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.
- Clark, P.J., Brzezinska, W.J., Thomas, M.W., Ryzhenko, N.A., Toshkov, S.A., & Rhodes, J.S. (2008). Intact neurogenesis is required for benefits of exercise on spatial memory but not motor performance or contextual fear conditioning in C57BL/6J mice. *Neuroscience*, *155*, 1048-1058.

- Colcombe, S., & Kramer, A.F. (2003). Fitness effects on the cognitive function of older adults: a meta-analytic study. *Psychological Science, 14*, 125-130.
- Colcombe, S.J., Kramer, A.F., Erickson, K.I., Scalf, P., McAuley, E., Cohen, N.J., ... & Elavsky, S. (2004). Cardiovascular fitness, cortical plasticity, and aging. *Proceedings of the National Academy of Sciences, 101*, 3316-3321.
- 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*, 563-570.
- Davranche, K., & Audiffren, M. (2004). Facilitating effects of exercise on information processing. *Journal of Sports Sciences, 22*, 419-428.
- Derrfuss, J., Brass, M., Neumann, J., & von Cramon, D.Y. (2005). Involvement of the inferior frontal junction in cognitive control: Meta-analyses of switching and Stroop studies. *Human Brain Mapping, 25*, 22-34.
- Diamond, A. (2013). Executive functions. *Annual Review of Psychology, 64*, 135-168.
- Fischer, B., & Weber, H. (1992). Characteristics of “anti” saccades in man. *Experimental Brain Research, 89*, 415-424.
- Gajewski, P.D., Hanisch, E., Falkenstein, M., Thönes, S., & Wascher, E. (2018). What does the n-back task measure as we get older? Relations between working-memory measures and other cognitive functions across the lifespan. *Frontiers in Psychology, 9*, 2208.
- Gillen, C., & Heath, M. (2014). Target frequency influences antisaccade endpoint bias: evidence for perceptual averaging. *Vision Research, 105*, 151-158.
- Hallett, P.E. (1978). Primary and secondary saccades to goals defined by instructions. *Vision Research, 18*, 1279-1296.
- Hershey, T., Black, K.J., Hartlein, J., Braver, T.S., Barch, D.M., Carl, J.L., & Perlmuter, J.S. (2004). Dopaminergic modulation of response inhibition: an fMRI study. *Cognitive Brain Research, 20*, 438-448.
- Hillman, C.H., Kramer, A.F., Belopolsky, A.V., & Smith, D.P. (2006). A cross-sectional examination of age and physical activity on performance and event-related brain potentials in a task switching paradigm. *International Journal of Psychophysiology, 59*, 30-39.
- Hwang, J., Brothers, R.M., Castelli, D.M., Glowacki, E.M., Chen, Y.T., Salinas, M.M., ... & Calvert, H.G. (2016). Acute high-intensity exercise-induced cognitive enhancement and brain-derived neurotrophic factor in young, healthy adults. *Neuroscience Letters, 630*, 247-253.

- Kiesel, A., Steinhauser, M., Wendt, M., Falkenstein, M., Jost, K., Philipp, A.M., & Koch, I. (2010). Control and interference in task switching—A review. *Psychological Bulletin*, *136*, 849.
- Kirchner, W.K. (1958). Age differences in short-term retention of rapidly changing information. *Journal of Experimental Psychology*, *55*, 352.
- Knaepen, K., Goekint, M., Heyman, E.M., & Meeusen, R. (2010). Neuroplasticity—exercise-induced response of peripheral brain-derived neurotrophic factor. *Sports Medicine*, *40*, 765–801.
- Kramer, A.F., Hahn, S., McAuley, E., Cohen, N.J., Banich, M.T., Harrison, C., ... & Vakil, E. (2001). Exercise, aging and cognition: healthy body, healthy mind. *Human Factors Interventions for the Health Care of Older Adults*, 91-120.
- Lambourne, K., & Tomporowski, P. (2010). The effect of exercise-induced arousal on cognitive task performance: a meta-regression analysis. *Brain Research*, *1341*, 12–24.
- Lemaire, V., Koehl, M., Le Moal, M., & Abrous, D.N. (2000). Prenatal stress produces learning deficits associated with an inhibition of neurogenesis in the hippocampus. *Proceedings of the National Academy of Sciences*, *97*, 11032-11037.
- León-Domínguez, U., Martín-Rodríguez, J.F., & León-Carrión, J. (2015). Executive n-back tasks for the neuropsychological assessment of working memory. *Behavioural Brain Research*, *292*, 167-173.
- Li, L., Men, W.W., Chang, Y.K., Fan, M.X., Ji, L., & Wei, G.X. (2014). Acute aerobic exercise increases cortical activity during working memory: a functional MRI study in female college students. *PloS One*, *9*, e99222.
- 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*, 1611-1626.
- MacDonald, A.W., Cohen, J.D., Stenger, V.A., & Carter, C.S. (2000). Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science*, *288*, 1835-1838.
- MacLeod, C.M. (1992). The Stroop task: The "gold standard" of attentional measures. *Journal of Experimental Psychology: General*, *121*, 12.
- Mansouri, F.A., Buckley, M.J., Fehring, D.J., & Tanaka, K. (2019). The role of primate prefrontal cortex in bias and shift between visual dimensions. *Cerebral Cortex*, *00*, 1-15.

- McMorris, T., Sproule, J., Turner, A., & Hale, B.J. (2011). Acute, intermediate intensity exercise, and speed and accuracy in working memory tasks: a meta-analytical comparison of effects. *Physiology and Behavior*, *102*, 421-428.
- Ming, G.L., & Song, H. (2011). Adult neurogenesis in the mammalian brain: significant answers and significant questions. *Neuron*, *70*, 687-702.
- Monsell, S. (2003). Task switching. *Trends in Cognitive Sciences*, *7*, 134-140.
- Moore, C.I., & Cao, R. (2008). The hemo-neural hypothesis: on the role of blood flow in information processing. *Journal of Neurophysiology*, *99*, 2035-2047.
- Munoz, D.P., & Everling, S. (2004). Look away: the anti-saccade task and the voluntary control of eye movements. *Nature Reviews Neuroscience*, *5*, 218-228.
- Ogoh, S., & Ainslie, P.N. (2009). Regulatory mechanisms of cerebral blood flow during exercise: new concepts. *Exercise and Sport Sciences Reviews*, *37*, 123-129.
- Owen, A.M., McMillan, K.M., Laird, A.R., & Bullmore, E. (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Human Brain Mapping*, *25*, 46-59.
- Padilla, C., Pérez, L., & Andrés, P. (2014). Chronic exercise keeps working memory and inhibitory capacities fit. *Frontiers in Behavioral Neuroscience*, *8*, 49.
- Padilla, C., Pérez, L., Andrés, P., & Parmentier, F.B. (2013). Exercise improves cognitive control: evidence from the stop signal task. *Applied Cognitive Psychology*, *27*, 505-511.
- Pierrot-Deseilligny, C., Rivaud, S., Gaymard, B., Müri, R., & Vermersch, A.I. (1995). Cortical control of saccades. *Annals of Neurology*, *37*, 557-567.
- Royall, D.R., Lauterbach, E.C., Cummings, J.L., Reeve, A., Rummans, T.A., Kaufer, D.I., ... & Coffey, C.E. (2002). Executive control function: a review of its promise and challenges for clinical research. A report from the Committee on Research of the American Neuropsychiatric Association. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *14*, 377-405.
- Stroop, J.R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology*, *18*, 643-662.
- Stuss, D.T., Floden, D., Alexander, M.P., Levine, B., & Katz, D. (2001). Stroop performance in focal lesion patients: dissociation of processes and frontal lobe lesion location. *Neuropsychologia*, *39*, 771-786.
- Tari, B., Fadel, M.A., & Heath, M. (2019). Response suppression produces a switch-cost for spatially compatible saccades. *Experimental Brain Research*, *237*, 1195-1203.



- Tari, B., & Heath, M. (2019). Pro-and antisaccade task-switching: response suppression—and not vector inversion—contributes to a task-set inertia. *Experimental Brain Research*, 1-10.
- Themanson, J R., Hillman, C.H., & Curtin, J.J. (2006). Age and physical activity influences on action monitoring during task switching. *Neurobiology of Aging*, 27, 1335-1345.
- Tomprowski, P.D., & Ganio, M.S. (2006). Short-term effects of aerobic exercise on executive processing, memory, and emotional reactivity. *International Journal of Sport and Exercise Psychology*, 4, 57-72.
- Truelle, J.L., Le Gall, D., Joseph, P.A., & Aubin, G. (1995). Movement disturbances following frontal lobe lesions: qualitative analysis of gesture and motor programming. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology*, 8, 14-19.
- Tsai, C.L., Pan, C.Y., Chen, F.C., Wang, C.H., & Chou, F.Y. (2016). Effects of acute aerobic exercise on a task-switching protocol and brain-derived neurotrophic factor concentrations in young adults with different levels of cardiorespiratory fitness. *Experimental Physiology*, 101, 836-850.
- van Praag, H. (2008). Neurogenesis and exercise: past and future directions. *Neuromolecular Medicine*, 10, 128-140.
- Weiler, J., Hassall, C.D., Krigolson, O.E., & Heath, M. (2015). The unidirectional prosaccade switch-cost: electroencephalographic evidence of task-set inertia in oculomotor control. *Behavioural Brain Research*, 278, 323-329.
- Weiler, J., & Heath, M. (2012a). The prior-antisaccade effect influences the planning and online control of prosaccades. *Experimental Brain Research*, 216, 545-552.
- Weiler, J., & Heath, M. (2012b). Task-switching in oculomotor control: unidirectional switch-cost when alternating between pro-and antisaccades. *Neuroscience Letters*, 530, 150-154.
- Weiler, J., & Heath, M. (2014a). Oculomotor task switching: alternating from a nonstandard to a standard response yields the unidirectional prosaccade switch-cost. *Journal of Neurophysiology*, 112, 2176–2184.
- Weiler, J., & Heath, M. (2014b). Repetitive antisaccade execution does not increase the unidirectional prosaccade switch-cost. *Acta Psychologica*, 146, 67-72.
- Weiler, J., Mitchell, T., & Heath, M. (2014). Response suppression delays the planning of subsequent stimulus-driven saccades. *PLoS One*, 9, e86408.
- Wurtz, R.H., & Albano, J.E. (1980). Visual-motor function of the primate superior colliculus. *Annual Review of Neuroscience*, 3, 189-226.

- Wylie, G., & Allport, A. (2000). Task switching and the measurement of “switch costs”. *Psychological Research*, 63, 212-233.
- Yanagisawa, H., Dan, I., Tsuzuki, D., Kato, M., Okamoto, M., Kyutoku, Y., & Soya, H. (2010). Acute moderate exercise elicits increased dorsolateral prefrontal activation and improves cognitive performance with Stroop test. *NeuroImage*, 50, 1702-1710.
- Zelazo, P.D., Blair, C.B., & Willoughby, M.T. (2016). *Executive function: Implications for education (NCER 2017-2000)*. Washington, DC: National Center for Education Research, Institute of Education Sciences, U.S. Department of Education.

## Chapter 2

A single bout of moderate-to-heavy intensity exercise improves task-switching efficiency

## 2.1 Introduction

A single bout of aerobic and/or resistance exercise improves cognition (Etnier, Nowell, Landers, & Sibley, 2006) and provides the largest and most reliable benefit to executive function (for meta analyses see Chang, Labban, Gapin, & Etnier, 2012; Lambourne & Tomporowski, 2010). Executive function represents a constellation of cognitive processes including: (1) response inhibition (2) working memory, and (3) cognitive flexibility (Diamond, 2013). Notably, executive function is mediated via an extensive frontoparietal network (for review see Nowrangi, Lyketsos, Rao, & Munro, 2014) that demonstrates improved task-dependent activity following single bout (Hillman, Snook, & Jerome, 2003) and chronic (Colcombe et al., 2004) exercise. For example, Scudder and colleagues (Scudder, Drollette, Pontifex, & Hillman, 2012) reported that a single bout of aerobic exercise (30-min at 60% of predicted maximal heart rate:  $HR_{max}$ ) improved behavioural measures of executive performance and was associated with a concurrent increase in the amplitude of P300 event-related brain potential (ERP) – a waveform thought to reflect executive control (Donchin & Coles, 1988). This post-exercise improvement has been linked to increased brain-derived neurotrophic factor (BDNF) (for mechanism see Dinoff, Herrmann, Swardfager, & Lanctôt, 2017) and catecholamine (Winter et al., 2007) concentration, and/or increased regional cerebral blood flow (for mechanism see Ogoh & Ainslie, 2009) that serves to improve neural efficiency (for review see Anish, 2005).

The majority of work identifying a single bout exercise benefit to executive function has employed response inhibition (e.g., Stroop and flanker tasks) and working memory (e.g., AX-continuous performance and n-back tasks) (Chang et al., 2012). It is therefore largely unclear whether additional components of executive function such as cognitive flexibility similarly benefit from a single bout of exercise. Diamond (2013) proposed that cognitive flexibility reflects the flexible allocation of one task to the next (i.e., task-switching) and that the rapid alternation between tasks represents a critical activity of daily living and inefficient performance can be used as a biomarker for cognitive decline (Schmitter-Edgecombe & Sanders, 2009). One method used to measure the executive costs of cognitive flexibility is the task-switching paradigm. In this paradigm, participants alternate between different tasks after every second trial (i.e., AABB) and the alternation from one task to the next typically results in longer reaction times (RT) and decreased response accuracy (i.e., a task-switch cost) (Allport, Styles, & Hsieh, 1994). To our knowledge, only a limited number of studies have examined exercise-related

changes to cognitive flexibility and the results of this work are equivocal. Some work has reported a post-exercise benefit (e.g., Hillman, Kramer, Belopolsky, & Smith, 2006; Kamijo & Takeda, 2010; Kramer et al., 1999; Tsai, Pan, Chen, Wang, & Chou, 2016), whereas others have not (Coles & Tomporowski, 2008; Kubesch et al., 2003; Tomporowski, Davis, Lambourne, Gregoski, & Tkacz, 2008; Tomporowski & Ganio, 2006). It is, however, important to recognize that the aforementioned studies employed task-switching paradigms requiring the alternation between parity (e.g., odd/even), size (e.g., low/high), or consonant/vowel judgments; that is, the tasks entail perceptual judgments that engage non-executive control processes. For example, Tsai et al. (2016), asked participants to perform a 30-min single bout of exercise (via treadmill) at 60% of their  $VO_{2max}$  and pre- and post-exercise executive function was assessed via a task wherein participants completed parity and size judgments in an AABB paradigm (i.e., A=parity judgment and B=size judgment). Tsai et al. reported a 58 ms post-exercise reduction in the magnitude of a task-switch cost – a result the authors interpreted to reflect an exercise-related improvement in executive function<sup>1</sup>. In contrast, Tomporowski & Ganio (2006) employed a 30-min aerobic exercise protocol (via cycle ergometer) at 60%  $VO_{2max}$  and ordered odd/even and vowel/consonant judgments tasks in an AABB paradigm. Results showed that the exercise intervention did not modulate the magnitude of a task-switching cost. Accordingly, it is unclear whether exercise reliably improves cognitive flexibility.

Experiment 1 of the present work examined whether a 20-min single bout of aerobic exercise (via cycle ergometer) performed at a moderate-to-heavy intensity (80% of  $HR_{max}$ ) differentially influences pre- and post-exercise pro- and antisaccade performance when ordered in an AABB paradigm (i.e., A=prosaccade, B=antisaccade). Experiment 2 involved a 20-min ‘rest’ interval (i.e., participants sat on the cycle ergometer without exercising) and was used to determine whether any pre- to post- changes in pro- and antisaccade performance were exercise-specific or reflected a task-related practice improvement. Notably, pro- and antisaccades were used here because they are mediated independent of the non-executive components of language and numerosity judgments associated with previous task-switching studies. As such, the present work provides a more direct and subtle measure to identify putative exercise-related benefits to

<sup>1</sup> Tsai et al. (2016) included separate groups of participants who were classified as being higher- (i.e.,  $VO_{2max} > 75^{th}$  percentile) and lower- (i.e.,  $VO_{2max} < 75^{th}$  percentile) fit. The authors reported a post-exercise reduction in task-switch-costs for the high-fit group but not the low-fit group. This result is consistent with some evidence that higher-fit individuals accrue a larger magnitude post-exercise benefit to executive function (Chang et al. 2012), but is not in keeping with a recent meta-analysis arguing that low- and higher-fit individuals accrue a similar post-exercise benefit to executive function (Ludygda et al., 2016).

the top-down executive control of attentional reallocation/cognitive flexibility. In particular, prosaccades are a standard oculomotor task (i.e., overlapping stimulus-response (SR) spatial relations) requiring a saccade to the veridical location of a target and are mediated via direct retinotopic projections in the superior colliculus (Wurtz & Albano, 1980) that operate largely independent of executive planning mechanisms (Pierrot-Deseilligny, Rivaud, Gaymard, Müri, & Vermersch, 1995). In contrast, antisaccades are a non-standard task (i.e., decoupled SR spatial relations) requiring that an individual saccade mirror-symmetrical (i.e., 180° spatial transformation) to a target. Antisaccades have longer RTs (Hallett, 1978), more directional errors (Fischer & Weber, 1992) and less accurate and more variable endpoints than their prosaccade counterparts (Dafoe, Armstrong, & Munoz, 2007; Gillen & Heath, 2014). The antisaccade behavioural ‘costs’ have been shown to reflect the executive demands of suppressing a stimulus-driven prosaccade (i.e., response suppression) and the visual remapping of a target’s coordinates (i.e., vector inversion) (for review see Munoz & Everling, 2004). Extensive neuroimaging and electrophysiological evidence in humans and non-human primates have linked the executive components of response suppression and vector inversion to the same frontoparietal circuitry that show task-dependent changes in activity following single bout and chronic exercise interventions (e.g., Brown, Vilis, & Everling, 2007; Colcombe et al., 2004; Curtis & D’Esposito, 2003; DeSouza, Menon, & Everling, 2003). Accordingly, the known neuroanatomical correlates of pro- and antisaccades coupled with the task’s hands-, language-, and numerical-free nature, and the resolution of eye-tracking technology (i.e., 1000 Hz), provide an optimal framework for examining exercise-related task-switching benefits.

Previous work by our group (Tari, Fadel, & Heath, 2019; Weiler, Hassall, Krigolson, & Heath, 2015; Weiler & Heath, 2012a, 2012b, 2014a, 2014b; Weiler, Mitchell, & Heath, 2014) reported that RTs for a prosaccade preceded by an antisaccade (i.e., task-switch trial) produce longer RTs than when preceded by its same task-type counterpart (i.e., task-repeat trial), whereas RTs for antisaccade task-switch and task-repeat trials do not reliably differ (i.e., the *unidirectional prosaccade switch-cost*). In accounting for these findings, our group has drawn upon the task-set inertia hypothesis’ assertion that the executive demands of planning an antisaccade renders the activation of a non-standard and executive mediated task-set that persists inertially and proactively interferes with the planning of a subsequent standard prosaccade response (Allport et al., 1994; see also Wylie & Allport, 2000). In turn, the task-set inertia

hypothesis contends that switching from a standard to a non-standard task (e.g., from a prosaccade to an antisaccade) does not engender a switch-cost because the former operates independent of an executive-mediated task-set. The task-set inertia hypothesis is supported by neuroimaging evidence reporting that a non-standard task results in increased frontoparietal activity as compared to a standard task (Derrfuss, Brass, Neumann, & von Cramon, 2005; Li, Wang, Zhao, & Fogelson, 2012; Nee, Wager, & Jonides, 2007; Yeung, Nystrom, Aronson, & Cohen, 2006), and work demonstrating that the amplitude of the P300 ERP for task-switch prosaccades is comparable to task-repeat and task-switch antisaccades and is different in amplitude from task-repeat prosaccades (Weiler et al., 2015). Accordingly, if a single bout of aerobic exercise improves neural efficiency in the executive networks mediating task-switching (and hence cognitive flexibility) then Experiment 1 should demonstrate that the magnitude – or perhaps presence – of the unidirectional prosaccade switch-cost is reduced post-exercise. Moreover, Experiment 2 demonstrates a consistent magnitude switch-cost across pre- and post-break assessments then results would provide convergent evidence that a single bout of aerobic exercise improves the flexible allocation of attention.

## 2.2 Methods

### 2.2.1 Experiment 1

#### *Participants*

The sample size of 20 participants was based on a power level of .80 (alpha = .05, two-tailed) with a standard deviation and effect size estimate derived from an earlier study by our group (Samani & Heath, 2018). Twenty participants (11 female and 9 male: age range 18-25 years) from University of Western Ontario community volunteered for this experiment. All participants had normal or corrected-to-normal vision, declared being right-hand dominant, and reported no history of neurological impairment or eye injury. All participants attained a full score on the Physical Activity Readiness Questionnaire (PAR-Q) and completed the Godin Leisure-Time Exercise Questionnaire (GLETQ) (Godin, 2011). The group mean score on the GLETQ was 65 (SD = 17: Range = 38-98) and indicates that participants could be classified as recreationally *active* (Amireault, Godin, Lacombe, & Sabiston, 2015).

Participants abstained from strenuous exercise, alcohol and caffeine consumption 12 hr prior to the protocol described below and were encouraged to get eight hours of sleep the night before data collection. Participants signed a consent form approved by the Health Sciences Research Ethics Board, University of Western Ontario, and this study was conducted in accordance with the Declaration of Helsinki.

### *Exercise Intervention*

During the exercise intervention participants sat on a height adjustable 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). The monitor was used to ensure participants exercised within the prescribed intensity level (see details below). Participants completed a single exercise intervention that entailed a 2.5 min warm-up in which heart rate was less than 50% of predicted maximal heart rate (i.e.,  $HR_{max}$ ; 220-minus age). Following the warm-up, participants exercised at a moderate-to-heavy intensity (i.e., 80% of  $HR_{max}$ ) for 20 min. The definition for moderate-to-heavy intensity was adopted from the Surgeon General's Report on Physical Activity and Health (United States, Department of Health, and Human Services, 1996). Moreover, the intensity level used here was based on previous work by our group showing that a post-exercise benefit to inhibitory control mechanisms can be observed across a continuum of moderate to very-heavy intensity exercise intensities (i.e., 80% of lactate threshold to 50% of the difference between lactate threshold and  $VO_{2peak}$ ) (Heath et al., 2018; Petrella, Belfry, & Heath, 2019). When heart rate fell above or below the desired beats per minute, participants were instructed to adjust the resistance on the cycle ergometer accordingly. Following the 20-min exercise period participants cooled down for 2.5 min at the same wattage used in the warm-up session.

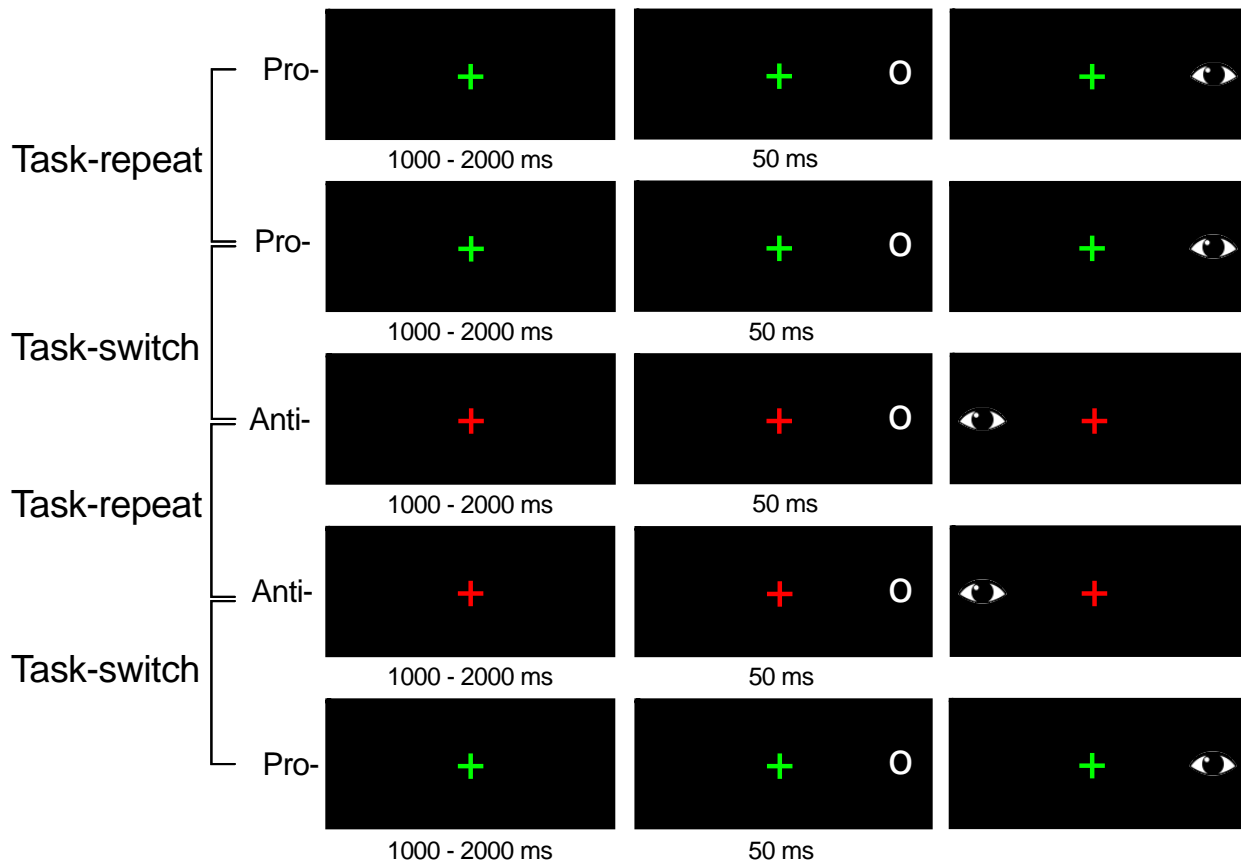
### *Oculomotor Task*

Prior to and after the exercise session participants completed an oculomotor assessment. For this assessment, participants sat in a height adjustable chair in front of a table (760 mm in height) with their head placed in a head/chin rest. Visual stimuli were presented on a 30-inch LCD monitor (60 Hz, 8 ms response rate, 1280 x 960 pixels; Dell 3007WFP, Round Rock, TX, USA) placed 550 mm from the front edge of the tabletop and centred on participant's midline. The gaze location of participants' left eye was measured via a video-based eye-tracking system (EyeLink 1000 Plus, SR Research, Ottawa, ON, Canada) sampling at 1000 Hz. Two additional



monitors provided real-time point of gaze information, trial-by-trial saccade kinematics (e.g., displacement, velocity), and monitored the accuracy of the eye-tracking system (i.e., to perform a recalibration if necessary). Prior to data collection a nine-point calibration of the viewing space was performed and confirmed via an immediate follow-up validation (i.e.,  $<1^\circ$  of error for each of the nine points in the calibration grid). Computer events were controlled via MATLAB (R2018b, The MathWorks, Natick, MA, USA) and the Psychophysics Toolbox extensions (v 3.0) (Brainard, 1997; Kleiner, Brainard, & Pelli, 2007) including the Eyelink Toolbox (Cornelissen, Peters, & Palmer, 2002). The lights in the experimental suite were extinguished during data collection.

Visual stimuli were presented on a high-contrast black background ( $0.1 \text{ cd/m}^2$ ). Stimuli included a green and a red fixation cross ( $1.0^\circ$ ) that were luminance matched ( $42 \text{ cd/m}^2$ ) and centered horizontally on the monitor at participants' eye level. In addition, open white circles ( $136 \text{ cd/m}^2$ ;  $2.5^\circ$  in diameter) served as targets and were presented  $13.5^\circ$  (i.e., proximal) and  $17.5^\circ$  (i.e., distal) to the left or right – and in the same horizontal meridian – of the fixation cross. A trial began with the presentation of a green or a red fixation cross which instructed participants to direct their gaze to its location. The colour of the fixation cross indicated the nature of the upcoming trial. For half of the participants the green fixation cross indicated a prosaccade (i.e., saccade to veridical target location), whereas the red fixation cross indicated an antisaccade (i.e., saccade mirror-symmetrical to target location) (see **Figure 2**). For the other half of participants, the converse fixation colour-to-task mapping was used. Once a stable gaze was achieved (i.e.,  $\pm 1.5^\circ$  for 450 ms), a uniformly distributed randomized foreperiod (1000-2000 ms) was initiated during which time the fixation cross remained visible (i.e., overlap paradigm). We used an overlap paradigm to reduce the frequency of antisaccade directional errors (Munoz & Everling, 2004) given that the primary metric for this study was RTs for directionally correct pro- and antisaccades. Following the foreperiod, a target was presented for 50 ms after which time the target and fixation were extinguished. The onset of the target cued participants to pro- or antisaccade “as quickly and accurately as possible”. A brief target presentation was used to equate pro- and antisaccades for the absence of extraretinal feedback (Heath, Weiler, Marriott, & Welsh, 2011)



**Figure 2.** Schematic of visual events across five successive trials. Participants alternated between pro- and antisaccades after every second trial (i.e., AABB). In this schematic, the green fixation cross denotes a saccade to the target’s veridical location (i.e., prosaccade), whereas the red fixation cross cued a saccade to the target’s mirror-symmetrical (i.e., antisaccade) location. For usability the schematic depicts only a single target eccentricity presented to the right of fixation; however, in the current investigation the target eccentricity (i.e., 13.5° and 17.5°) and target location (i.e., left and right of fixation) were pseudo-randomized.

Participants alternated between pro- and antisaccades after every second trial (i.e., AABB: A=prosaccade, B=antisaccade) at pre- and post-exercise assessments. Each assessment included a single block of 160 trials equally divided into 80 task-repetition (i.e., pro- or antisaccade preceded by its same task counterpart) and 80 task-switch (i.e., prosaccade preceded by an antisaccade or vice versa) pro- and antisaccade trials. The target location (i.e., left and right; proximal and distal) was pseudo-randomly ordered in one of four predetermined trial sequences that could not be predicted by participants. The task-type (pro- vs. antisaccade)

associated with the first trial of an oculomotor session was counterbalanced, and because the first trial was neither a task-switch nor a task-repetition it was excluded from further data analyses.

Following the pre-exercise oculomotor assessment participants immediately completed their 20-min aerobic exercise session. Following the exercise session, the post-exercise oculomotor assessment was completed. The post-exercise assessment was completed between two and four minutes following the cool-down period and occurred only after participants' heart rate was less than 100 beats per minute. Each oculomotor assessment required 15-17 min to complete (including calibration prior to data collection). The timing and length of our post-exercise assessment was based on work (Chang et al., 2012) showing that the largest exercise-related executive benefit occurs within 20-min post-exercise.

#### *Data reduction, dependent variables, and statistical analysis*

Point of gaze 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 and acceleration. Saccade onset was determined via velocity and acceleration values that exceeded  $30^\circ/\text{s}$  and  $8000^\circ/\text{s}^2$ , respectively. Saccade offset was determined when velocity fell below  $30^\circ/\text{s}$  for 40 ms. Trials with missing data (e.g., blinks, signal loss) were excluded as were trials with: (1) an anticipatory response (i.e.,  $\text{RT} < 85$  ms), (2) a RT greater than 2.5 times the interquartile range of a participant- and condition-specific median, and (3) an amplitude less than  $2^\circ$  or greater than 2.5 standard deviations above a participant- or condition-specific mean (Weiler & Heath, 2014a). Less than 8% of trials were removed for the aforementioned criteria. Further, trials involving a directional error (i.e., a prosaccade instead of an instructed antisaccade or vice versa) were excluded from the computation of the dependent variables listed below. The basis for this is that a trial involving an antisaccade directional error engages response planning mechanisms distinct from their directionally correct counterparts (DeSimone, Weiler, Aber, & Heath, 2014). Only 1% and 4% of pro- and antisaccades, respectively, entailed a directional error. The low error rate is attributed to the predictable nature of the AABB paradigm used here.

Dependent variables were: reaction time (RT: time from target presentation to saccade onset), the interquartile range (IQR) of RT, movement time (MT: time from movement onset to movement offset), and saccade amplitude and amplitude variability in the primary (i.e., horizontal) movement direction. Given the positive skew of RT distributions (see **Figure 3**),

participant-specific median RT values (and associated interquartile range) were used, whereas mean MT and amplitude (and associated within-participant standard deviations) were used. Dependent variables were examined via 2 (time: pre- and post-exercise) by 2 (task: prosaccade, antisaccade) by 2 (task-transition: task-switch, task-repeat) by 2 (target eccentricity: 13.5° [proximal], 17.5° [distal]) fully repeated measures ANOVA. An alpha level of 0.05 was set for all statistical comparisons and simple effects were used for post-hoc contrasts.

## 2.2.2 Experiment 2

### *Participants*

The sample size of 15 participants was based on a power level of .80 (alpha =.05, two-tailed) with a standard deviation and effect size estimate derived from an earlier study by our group (Samani & Heath, 2018). Fifteen students (8 female and 7 male: age range 19-25 years) from the University of Western Ontario volunteered for this study and were independent of the participants recruited in Experiment 1. Experiment 2 involved the same inclusion criterion as Experiment 1. The minimum and maximum GLETQ scores were 30 and 98, respectively (Mean=59, SD=18) and did not reliably differ from Experiment 1 ( $t(29.3)=0.98$ ,  $p=.33$ ).

### *Control Intervention*

The same equipment and methods used in Experiment 1 were used here with the only exception that between the pre- and post-oculomotor assessments participants sat and rested on the cycle ergometer for 27 min (i.e., the average interval between the end of the pre-break and onset of the post-break oculomotor assessment in Experiment 1). In other words, Experiment 2 was a non-exercise control condition and was designed to determine whether any switch-cost changes noted post-exercise in Experiment 1 were exercise-specific or related to a practice related improvement in the pro- and antisaccade AABB paradigm. During the rest interval participants were able to use their personal mobile device and/or converse with the experimenter.

### *Data reduction, dependent variables, and statistical analysis*

The same data reduction techniques and dependent variables used in Experiment 1 were used here. Fewer than 6% of trials were removed due to the RT and amplitude criterion outlined in Experiment 1, and 2% and 9% of trials entailed a pro- and antisaccade directional error, respectively. For the ANOVA model, Experiment 2 employed pre- and post-break instead of the pre- and post-exercise nomenclature used in Experiment 1.

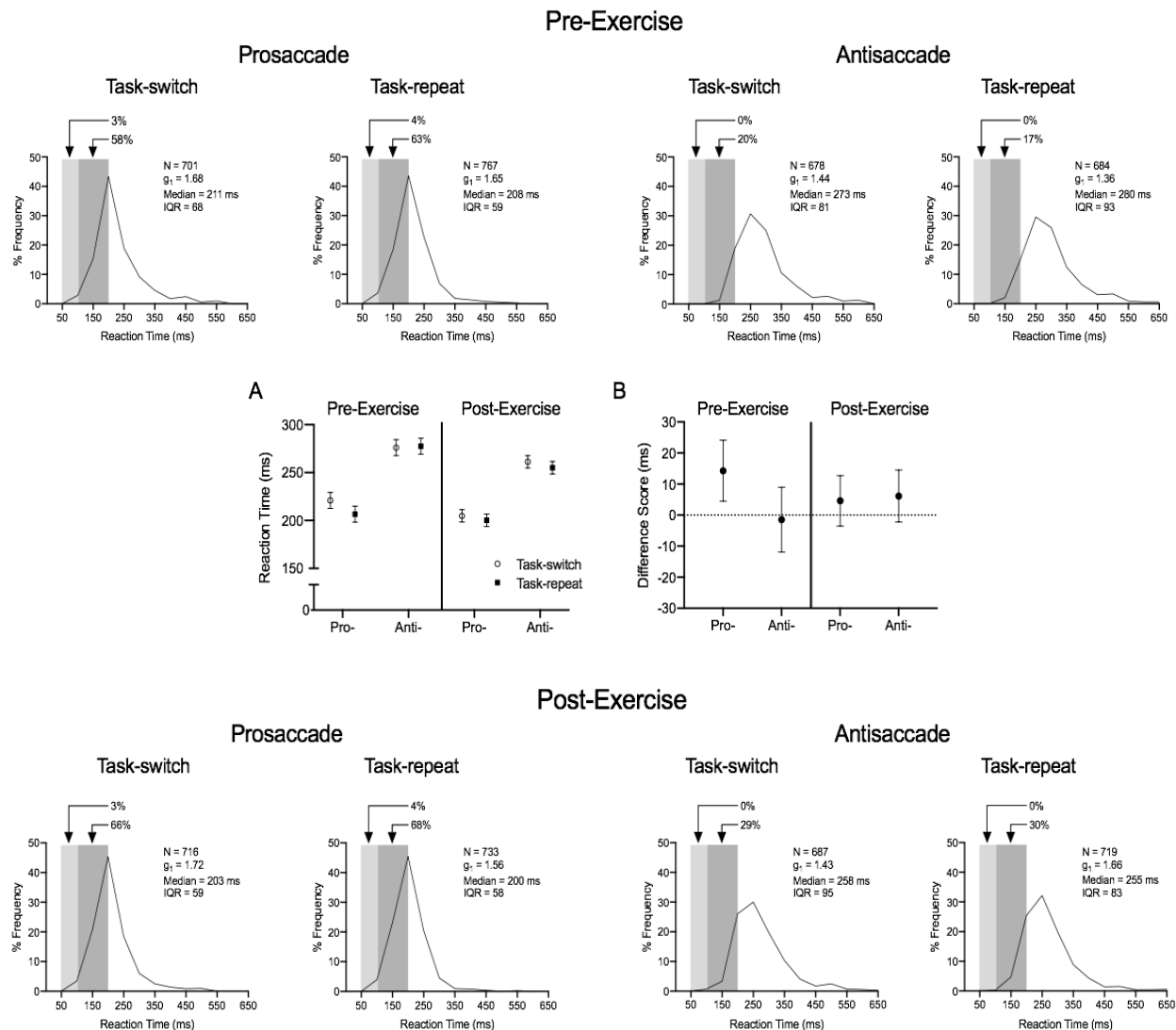
## 2.3 Results

### 2.3.1 Experiment 1

#### *Reaction time and reaction time variability*

The main panels of **Figure 3** show RT percent frequency histograms for pre- and post-exercise pro- and antisaccade task-switch and task-repeat trials. The light and darker grey rectangles represent bins for anticipatory (i.e., <100 ms) and short-latency (i.e., 100 to <200 ms) responses. Antisaccades did not produce anticipatory responses, whereas prosaccade trials did (although low in frequency), and as expected, antisaccades had fewer short-latency responses than prosaccades. Notably, however, **Figure 3** shows that the percentage of anticipatory and short-latency pro- and antisaccades did not demonstrate a marked pre- to post-exercise difference. In terms of quantitative analyses, RT produced main effects for time,  $F(1,19)=28.61$ ,  $p<.001$ ,  $\eta_p^2=.60$ , task,  $F(1,19)=67.88$ ,  $p<.001$ ,  $\eta_p^2=.78$ , task-transition,  $F(1,19)=8.28$ ,  $p=.01$ ,  $\eta_p^2=.30$ , and a three-way interaction involving each variable,  $F(1,19)=5.45$ ,  $p=.03$ ,  $\eta_p^2=.22$ . In decomposing the three-way interaction, **Figure 3a** shows that pre-exercise prosaccade task-switch RTs were longer than their task-repeat counterparts ( $t(19)=2.75$ ,  $p=.012$ ), whereas antisaccade task-switch and task-repeat trials did not reliably differ ( $t(19)=-0.26$ ,  $p=.80$ ). For the post-exercise assessment, pro- and antisaccade task-switch and task-repeat trials did not reliably differ (all  $t(19)=1.08$  and  $1.05$ ,  $ps>.29$ ). Given the nature of our research objective, we used two one-sided test (TOST) statistics (i.e., a test of equivalence) to examine null task-switch effects. Results showed that pre-exercise antisaccades as well as post-exercise pro- and antisaccade task-switch and task-repeat trials were within an equivalence boundary (all  $t(19)>2.58$ ,  $ps<.009$ ). In other words, null and equivalence testing support the contention that a unidirectional prosaccade switch-cost was observed pre-exercise but not post-exercise. In addition, we computed participant-specific RT switch-cost difference scores (task-switch minus task-repeat) separately for pre- and post-exercise pro- and antisaccades. **Figure 3b** shows that the prosaccade pre-exercise difference score was larger than its post-exercise counterpart ( $t(19)=2.17$ ,  $p=.042$ ), whereas antisaccade pre- and post-exercise difference scores did not vary ( $t(19)=-1.20$ ,  $p=.25$ ).

Analysis of the IQR of RT produced a main effect for task:  $F(1,19)=8.52$ ,  $p<.01$ ,  $\eta_p^2=.31$ : prosaccades (54 ms,  $SD=21$ ) were less variable than antisaccades (69 ms,  $SD=30$ ).



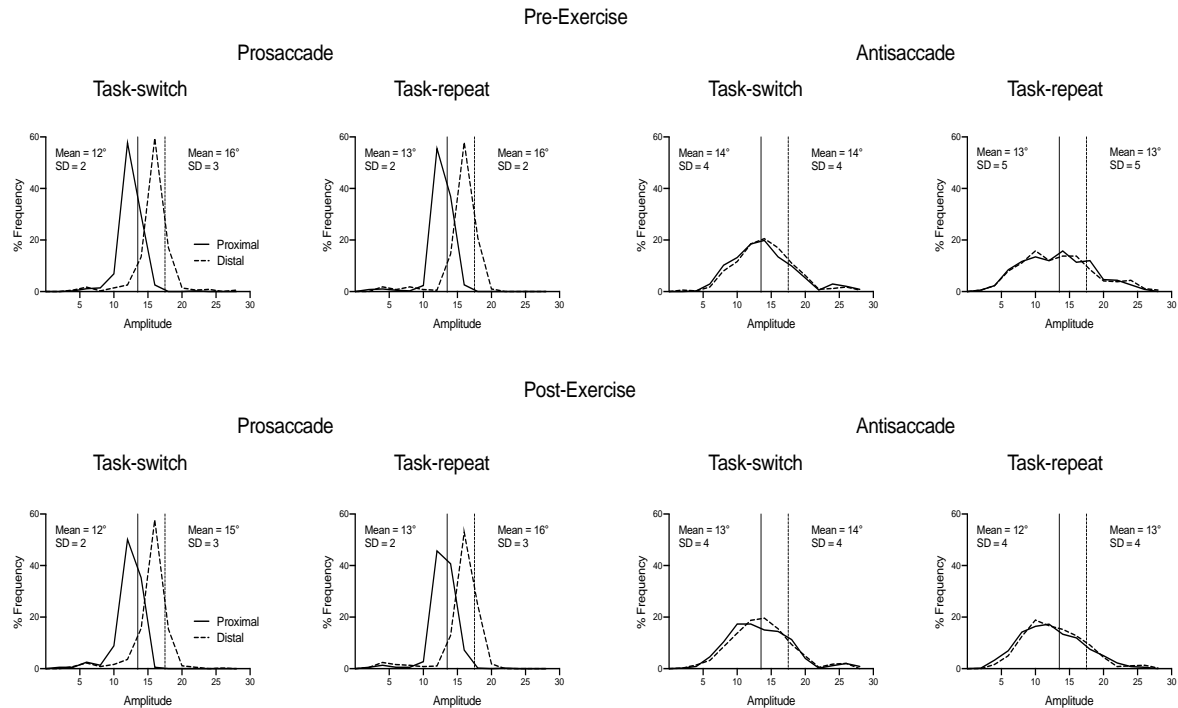
**Figure 3.** The main panels show pro- and antisaccade reaction time (ms) percent frequency histograms at pre- (top panels) and post-exercise (bottom panels) assessments for task-switch and task-repeat trials (bin widths of 50 ms). The inset left panel (A) shows group mean pro- and antisaccade task-switch and task-repeat reaction times (ms) at pre- and post-exercise assessments. Error bars represent 95% within-participant confidence intervals computed via the mean-squared error term for the task by task-transition interaction (Loftus & Masson, 1994). The inset right panel (B) shows group mean pro- and antisaccade reaction time difference scores (i.e., task-switch minus task-repeat) at pre- and post-exercise assessments. Error bars represent 95% between-participant confidence intervals. The absence of overlap between an error bar and zero (i.e., the horizontal line) represents a reliable effect inclusive to a test of the null hypothesis (Cumming, 2013).

### *Movement Time and Amplitude*

Results for MT produced a main effect of task,  $F(1,19)=17.43$ ,  $p=.001$ ,  $\eta_p^2=.48$ , target,  $F(1,19)=74.33$ ,  $p<.001$ ,  $\eta_p^2=.80$ , and their interaction,  $F(1,19)=49.07$ ,  $p<.001$ ,  $\eta_p^2=.72$ . Prosaccade MTs increased from the proximal (49 ms,  $SD=4$ ) to distal (55 ms,  $SD=5$ ) target ( $t(19)=-13.56$ ,  $p<.001$ ), whereas antisaccade MTs did not (proximal: 62 ms,  $SD=12$ ; distal: 62 ms,  $SD=11$ ) ( $t(19)=-.75$ ,  $p=.47$ ).

The main panels of **Figure 4** present amplitude percent frequency histograms for pre- and post-exercise pro- and antisaccade task-switch and task-repeat trials to the proximal and distal targets. The figure shows that prosaccade amplitudes increased in relation to target eccentricity, whereas antisaccades amplitudes did not. Moreover, the histograms provide the expected finding that antisaccade amplitudes were more variable than prosaccades – a finding that was consistent across pre- and post-exercise task-switch and task-repeat trials. Quantitative analysis revealed a main effect for target eccentricity,  $F(1,19)=410.76$ ,  $p<.001$ ,  $\eta_p^2=0.96$ , and a task by target eccentricity interaction,  $F(1,19)=219.93$ ,  $p<.001$ ,  $\eta_p^2=.92$ . Prosaccade amplitudes reliably increased from the proximal to the distal target ( $t(19)= 24.85$ ,  $p<.001$ ), whereas the scaling of antisaccade amplitudes to target eccentricity approached – but did not attain – a conventional level of statistical significance ( $t(19)= 1.91$ ,  $p=.07$ ).

Results for the variability of saccade amplitudes produced main effects for task,  $F(1,19)=48.11$ ,  $p<.001$ ,  $\eta_p^2=.72$ , target eccentricity,  $F(1,19)=8.86$ ,  $p<.01$ ,  $\eta_p^2=.32$ , and their interaction,  $F(1,19)=10.21$ ,  $p<.01$ ,  $\eta_p^2=.35$ . Prosaccade amplitudes for the proximal target ( $1.3^\circ$ ,  $SD=0.6$ ) were less variable than the distal target ( $1.9^\circ$ ,  $SD=0.9$ ) ( $t(19)= 3.97$ ,  $p<0.001$ ), whereas antisaccade proximal ( $2.8^\circ$ ,  $SD=0.7$ ) and distal ( $2.8^\circ$ ,  $SD=0.7$ ) targets produced endpoint variability that did not reliably differ ( $t(19)=-0.12$ ,  $p=.91$ ).



**Figure 4.** The main panels show pro- and antisaccade saccade amplitude percent frequency histograms at pre- (top panels) and post-exercise (bottom panels) assessments for task-switch and task-repeat trials to the proximal (i.e., 13.5°) and distal (i.e., 17.5°) targets eccentricities (bin widths of 2°). The vertical solid and dashed lines represent veridical locations for proximal and distal targets, respectively. The figure provides a qualitative demonstration that amplitudes for prosaccades – but not antisaccades – increased in relation to target eccentricity.

### 2.3.2 Experiment 2

#### *Reaction time and reaction time variability*

RT yielded a main effect for task,  $F(1,14)=40.84$ ,  $p<.001$ ,  $\eta_p^2=.74$ , and a task by task-transition interaction,  $F(1,14)=12.04$ ,  $p=.004$ ,  $\eta_p^2=.46$ . **Figure 5a** shows that RTs for prosaccade task-switch trials were longer than their task-repeat counterparts ( $t(14)=3.56$ ,  $p=.003$ ), whereas antisaccade task-switch and task-repeat trials did not differ ( $t(14)=-1.57$ ,  $p=.138$ ) and the TOST statistic indicated that RTs for the former approached – but did not attain – a conventional boundary of statistical equivalence ( $t(14)=1.52$ ,  $p=.076$ ). Results did not yield a time by task by task-transition interaction,  $F(1,14)=0.13$ ,  $p=.72$ ,  $\eta_p^2<.01$ . Further, participant-specific



prosaccade RT difference scores (task-switch minus task-repeat) did not reliably differ at pre- and post-break assessments ( $t(14)=0.64$ ,  $p=.533$ ) and the TOST statistic indicated that they were within an equivalence boundary ( $t(14)=2.18$ ,  $p=.023$ ).

The average IQR of RT for pro- (77 ms,  $SD=38$ ) and antisaccades (79 ms,  $SD=30$ ) did not reliably differ,  $F(1,14)=.13$ ,  $p=.716$ ,  $\eta_p^2=.01$ , and this dependent variable did not produce any reliable main effects or interactions, all  $F(1,14)<1.04$ ,  $p>.32$ ,  $\eta_p^2<.07$ .

### *Movement Time and Amplitude*

MT produced main effects of task,  $F(1,14)=5.57$ ,  $p=.03$ ,  $\eta_p^2=.28$ , target eccentricity,  $F(1,14)=152.53$ ,  $p<.001$ ,  $\eta_p^2=.92$ , and their interaction,  $F(1,14)=6.89$ ,  $p=.02$ ,  $\eta_p^2=.33$ .

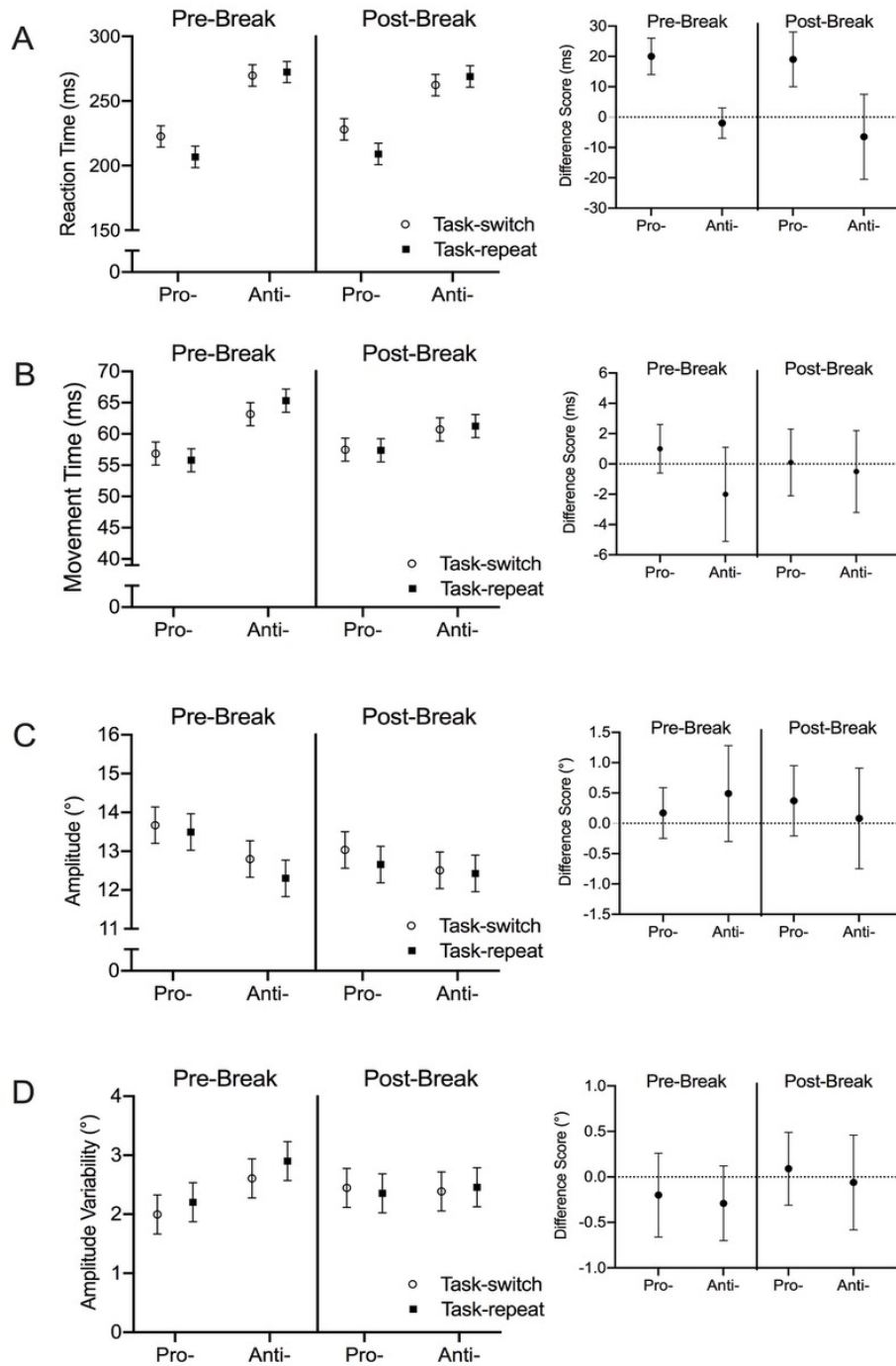
Prosaccade MTs increased from the proximal (54 ms,  $SD=8$ ) to distal (58 ms,  $SD=7$ ) target as did antisaccade MTs (proximal: 61 ms,  $SD=10$ ; distal: 64 ms,  $SD=9$ ) (all  $t(14)=6.90$  and  $4.94$ ,  $ps<.001$ ), and participant-specific target difference scores (distal target minus proximal target) revealed that the magnitude was larger for pro- than antisaccades ( $t(14)=2.62$ ,  $p=.020$ ).

Results for amplitude yielded a main effect of target eccentricity,  $F(1,14)=74.77$ ,  $p<.001$ ,  $\eta_p^2=.84$ , and a task by target eccentricity interaction,  $F(1,14)=18.67$ ,  $p=.001$ ,  $\eta_p^2=.57$ .

Prosaccade (proximal:  $12.0^\circ$ ,  $SD=1.0$ ; distal= $14.3^\circ$ ,  $SD=1.4$ ) and antisaccade (proximal:  $12.1^\circ$ ,  $SD=2.8$ ; distal= $12.8^\circ$ ,  $SD=2.8$ ) amplitudes increased with increasing target eccentricity ( $ts(14)=6.87$  and  $4.71$ ,  $ps<.001$ ), and participant-specific target difference scores (distal target minus proximal target) were larger for pro- than antisaccades ( $t(14)=4.32$ ,  $p=.001$ ).

Saccade amplitude variability produced main effects for task,  $F(1,14)=5.59$ ,  $p=.033$ ,  $\eta_p^2=.28$ , target eccentricity,  $F(1,14)=4.67$ ,  $p<.048$ ,  $\eta_p^2=.25$ , and their interaction,  $F(1,14)=5.84$ ,  $p=.030$ ,  $\eta_p^2=.29$ . Prosaccade amplitude variability was less for the proximal ( $1.9^\circ$ ,  $SD=0.6$ ) than distal target ( $2.5^\circ$ ,  $SD=0.9$ ) ( $t(19)=2.62$ ,  $p=0.020$ ), whereas antisaccade amplitude variability did not vary with target eccentricity (proximal:  $2.7^\circ$ ,  $SD=0.5$ ; distal:  $2.7^\circ$ ,  $SD=0.6$ ) ( $t(14)=-0.42$ ,  $p=.676$ ).

Last, **Figure 5** demonstrates that MT (**Figure 5b**), saccade amplitude (**Figure 5c**) and saccade amplitude variability (**Figure 5d**) did not elicit a time by task by task-transition interaction, all  $F(1,14)<2.44$ ,  $ps>.14$ ,  $\eta_p^2<.15$ . We note these null interactions because they demonstrate that saccade performance did not produce a reliable practice-related benefit.



**Figure 5.** The left panels depict group mean reaction time (A), movement time (B), saccade amplitude (C) and saccade amplitude variability (D) for pro- and antisaccade task-switch and task-repeat trials at pre- and post-break assessments. Error bars represent 95% within-participant confidence intervals. The right panels show pro- and antisaccade reaction time (A), movement time (B), saccade amplitude (C) and saccade amplitude variability (D) difference scores (task-

switch minus task-repeat) at pre- and post-break assessments. Error bars represent 95% between-participant difference scores.

## 2.4 Discussion

We sought to determine whether a single bout of moderate-to-heavy intensity aerobic exercise (i.e., 80% of predicted  $HR_{max}$ ) improves the efficiency of cognitive flexibility. To accomplish our objective, we employed a pro- and antisaccade task-switching paradigm. In addressing our findings, we first outline the general differences between pro- and antisaccades before discussing whether our exercise manipulation directly influenced task-switching efficiency.

### *Distinct planning mechanisms mediate pro- and antisaccades*

Antisaccades produced longer RTs and MTs and had more variable endpoints than their prosaccade counterparts – a finding independent of the AABB task-ordering and exercise intervention used here. The shorter prosaccade RTs reflect their mediation via direct retinotopic motor maps within the superior colliculus (SC) (Wurtz & Albano, 1980) that operate largely independent of top-down executive control (Pierrot-Deseilligny, Rivaud, Gaymard, & Agid, 1991). In turn, the longer antisaccade RTs are linked to increased activity in frontoparietal networks to support the task-set necessary to evoke the executive components of response suppression and vector inversion (Everling & Johnston 2013; see also Munoz & Everling, 2004). Additionally, that antisaccade MTs were longer than prosaccade and produced less accurate and more variable amplitudes is in accord with literature demonstrating that decoupling stimulus-response spatial relations increases uncertainty related to target location (Edelman & Goldberg, 2001) and results in motor output that is supported by visual information (i.e., relative) functionally distinct from the absolute visual information mediating prosaccades (Gillen & Heath 2014; Gillen, Weiler, & Heath, 2013; Heath, Gillen, & Weiler, 2015). Accordingly, the general differences between pro- and antisaccades provides a framework for contrasting stimulus-driven and executive-mediated oculomotor responses.

### *Exercise modulates the unidirectional prosaccade switch-cost*

Pre-exercise prosaccade task-switch RTs were longer than their task-repeat counterparts, whereas antisaccade task-switch and task-repeat RTs did not reliably differ. Put another way, pre-exercise performance was associated with a unidirectional prosaccade switch-cost and is in keeping with previous work by our group and others (Chan & DeSouza 2013; Heath et al., 2016; Tari et al., 2019; Weiler & Heath, 2012a, 2012b, 2014a, 2014b; Weiler et al., 2014, 2015). In terms of the switch-cost associated with our pre-exercise findings, it could be argued that task-repeat trials in an AABB paradigm may not serve as an appropriate control for evaluating a switch-cost because the second of two consecutively completed tasks may induce a task-repeat benefit (Wylie & Allport, 2000). In other words, RTs for task-repeat trials may be facilitated because they are preceded by their same task-type. In countering this view, we note that several purpose-designed studies have shown that RTs for prosaccades performed in a separate trial block do not differ from their task-repeat counterparts performed in an AABB paradigm (Weiler & Heath 2014b; Tari et al., 2019). As a result, RT difference between prosaccade task-switch and task-repeat trials is attributed to a switch-cost for the former trial-type. Moreover, the RT difference between prosaccade task-switch and task-repeat trials cannot be attributed to a difference in speed-accuracy relations (Fitts, 1954) given their comparable MT and endpoint properties. Accordingly, we propose that the longer RTs for task-switch prosaccades (i.e., the unidirectional prosaccade switch-cost) relates to the lingering neural activity necessary to evoke an antisaccade task-set (i.e., response suppression and/or vector inversion). In support of this view, Everling & Johnston's (2013) heterodox proposal asserts that excitatory inputs from the prefrontal cortex (PFC) to the SC are responsible for a task-set – or task-rules – necessary for the completion of a directionally correct antisaccade. It is thought that such a task-set persists inertially and delays the planning of a subsequent stimulus-driven prosaccade (Tari et al., 2019; Weiler & Heath, 2014a; Weiler et al., 2015).

In the post-exercise assessment, prosaccade *and* antisaccade task-switch trials did not differ from their task-repeat counterparts; that is, we did not observe a unidirectional prosaccade switch-cost. In particular, **Figure 3a** shows that the post-exercise difference between prosaccade task-switch and task-repeat trials was 3 ms – as opposed to the 25 ms difference observed during the pre-exercise intervention. Of course, a possible explanation for this finding is that the repeated oculomotor assessment engendered a practice-related improvement in task-set efficiency. To address this issue Experiment 2 provided a non-exercise control condition

wherein participants sat on the cycle ergometer for a period equivalent to the exercise intervention in between their pre- and post- oculomotor assessments. Results indicated a 19 ms and 20 ms unidirectional prosaccade switch-cost at pre- *and* post-break assessments and these values were within an equivalence boundary (i.e., TOST statistic). Furthermore, Experiment 2 findings for MT, saccade amplitude and amplitude variability generally mirrored those outlined for Experiment 1, and importantly, did not reliably differ across the pre- and post-break assessments<sup>2</sup>. Accordingly, we believe that a parsimonious explanation for the absence of a post-exercise unidirectional prosaccade switch-cost observed in Experiment 1 is that a single bout of aerobic activity increases neural efficiency within the PFC and allows for the more rapid dissipation of neural activity related to a non-standard (i.e., antisaccade) task-set. In support of this view, an ERP study focusing on response inhibition in a stop-signal task (Chu, Alderman, Wei, & Chang, 2015) found that 30-min of aerobic exercise at moderate intensity (65-75% of HR<sub>max</sub>) resulted in a larger amplitude P300 amplitude source-localized to PFC circuitry (Bledowski et al., 2004). These results suggest a task-dependent and exercise-related improvement in the efficiency of generating an executive-mediated stop-signal command. In terms of the mechanism associated with improved neural efficiency, Yanagisawa et al. (2010) showed that improved RT on the Stroop Interference task (i.e., an executive task) is associated with increased PFC cerebral oxygenation, and a systematic review (Knaepen, Goekint, Heyman, & Meeusen, 2010) reported that there is some evidence that acute aerobic exercise results in an increase in BDNF concentration which may in turn induce a cascade of neurotrophic and neuroprotective effects that are associated with improvements in executive function (Leckie et al., 2014). Moreover, Moore and Cao's (2008) hemo-neural hypothesis asserts that an increase in cerebral blood flow (e.g., via an exercise manipulation) leads to mechanical- and temperature-based changes to the brain's neural and glial networks that alters local cortical circuitry gains and improves the interneuronal communication supporting information processing. In other words, exercise may lead to transient mechanical changes to the brain that

<sup>2</sup> Antisaccade MT and saccade amplitude dependent variables scaled to target eccentricity in Experiment 2 but not Experiment 1. We are unsure of the nature of this discrepancy; however, it is important to recognize that Experiment 2 antisaccade MT and saccade amplitude scaling to target eccentricity was less than that associated with prosaccades. Moreover, both Experiments 1 and 2 indicated that MT and saccade amplitude did not reliably vary across pre- to post-exercise or pre- to post-break assessments.

improve executive function. Regardless of the neurophysiological mechanism, the present finding demonstrates that a single bout of exercise improves cognitive flexibility.

### *Study limitations*

Our study was limited to healthy young participants that reported an *active* lifestyle as determined via the GLETQ. It is therefore unclear whether a continuum of age and fitness levels would similarly exhibit an executive benefit. Thus, and although work by our group and others has suggested that exercise can improve response inhibition in older and less healthy adults (Johnson et al., 2016; Ludyga, Gerber, Brand, Holsboer-Trachsler, & Pühse, 2016; Petrella et al., 2019), it remains unclear whether such a finding can be extended to additional executive dimensions such as cognitive flexibility. Second, it is unclear how long the post-exercise improvement in cognitive flexibility persists. In the present work, executive function was measured within 20-min post-exercise and was based on Chang et al.'s (2012) assertion that the largest and most reliable executive benefit (largely related to inhibitory control) occurs within this time frame. That said, future work should examine whether the persistence of a post-exercise improvement to cognitive flexibility follows the same timeline as inhibitory control. Third, we employed only a moderate-to-heavy intensity exercise session over a 20-min exercise session. This manipulation was based on previous work by our group showing that a range of moderate (i.e., 80% of lactate threshold), heavy (i.e., 15% of the difference between lactate threshold and  $VO_{2peak}$ ) and very-heavy (i.e., 50% of the difference between lactate threshold and  $VO_{2peak}$ ) intensities completed across 10- and 20-min elicit a similar magnitude post-exercise improvement in response inhibition (i.e., Heath et al., 2018). We recognize that cognitive flexibility is an executive component distinct from response inhibition and that exercise-mediated changes in this function may render a distinct dose-response relationship. Our future work is designed to determine whether intensity and duration components differentially influence the post-exercise improvement in cognitive flexibility.

## 2.5 Conclusions

RTs for a prosaccade preceded by an antisaccade were longer than when preceded by their same task counterpart (i.e., unidirectional prosaccade switch-cost); however, this switch-cost was nullified following a 20-min single bout of moderate-to-heavy intensity exercise. Further, the results of a second experiment demonstrated that the absence of a post-exercise

switch-cost was unrelated to a practice-related improvement. Accordingly, exercise improved cognitive flexibility and is a finding that we propose to be – in part – related to enhanced neural efficiency within executive-mediated cortical networks.

## 2.6 References

- Allport, A., Styles, E.A., & Hsieh, S. (1994). *Shifting intentional set: exploring the dynamic control of tasks*, in: Umiltà, C., Moscovitch, M., (Eds.), *Attention and Performance XV*. MIT Press., Cambridge, pp. 421-452.
- Amireault, S., Godin, G., Lacombe, J., & Sabiston, C.M. (2015). The use of the Godin-Shepherd leisure-time physical activity questionnaire in oncology research: a systematic review. *BMC Medical Research Methodology*, *15*, 60.
- Anish, E.J. (2014). Exercise and its effects on the central nervous system. *Current Sports Medicine Reports*, *4*, 18-23.
- Bledowski, C., Prvulovic, D., Hoechstetter, K., Scherg, M., Wibral, M., Goebel, R., & Linden, D.E. (2004). Localizing P300 generators in visual target and distractor processing: a combined event-related potential and functional magnetic resonance imaging study. *Journal of Neuroscience*, *24*, 9353-9360.
- Brainard, D.H. (1997). The psychophysics toolbox. *Spatial Vision*, *10*, 433-436.
- Brown, M.R.G., Vilis, T., & Everling, S. (2007). Frontoparietal activation with preparation for antisaccades. *Journal of Neurophysiology*, *98*, 1751-1762.
- Chan, J.L., & DeSouza, J.F. (2013). The effects of attentional load on saccadic task switching. *Experimental Brain Research*, *227*, 301-309.
- 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.
- Clark, P.J., Brzezinska, W.J., Thomas, M.W., Ryzhenko, N.A., Toshkov, S.A., & Rhodes, J.S. (2008). Intact neurogenesis is required for benefits of exercise on spatial memory but not motor performance or contextual fear conditioning in C57BL/6J mice. *Neuroscience*, *155*, 1048-1058.
- Chu, C.H., Alderman, B.L., Wei, G.X., & Chang, Y.K. (2015). Effects of acute aerobic exercise on motor response inhibition: an ERP study using the stop-signal task. *Journal of Sport and Health Science*, *4*, 73-81.
- Colcombe, S.J., Kramer, A.F., Erickson, K.I., Scalf, P., McAuley, E., Cohen, N.J., ... & Elavsky, S. (2004). Cardiovascular fitness, cortical plasticity, and aging. *Proceedings of the National Academy of Sciences*, *101*, 3316-3321.

- Coles, K., & Tomporowski, P.D. (2008). Effects of acute exercise on executive processing, short-term and long-term memory. *Journal of Sports Sciences, 26*, 333-344.
- Cornelissen, F.W., Peters, E.M., & Palmer, J. (2002). The Eyelink toolbox: eye tracking with MATLAB and the psychophysics toolbox. *Behavior Research Methods, Instruments, and Computers, 34*, 613-617.
- Cumming, G. (2013). *Understanding the new statistics: effect sizes, confidence intervals, and meta-analysis*. New York, NY, US: Routledge/Taylor & Francis Group.
- Curtis, C.E., & D'Esposito, M. (2003). Success and failure suppressing reflexive behavior. *Journal of Cognitive Neuroscience, 15*, 409-418.
- 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*, 563-570.
- Derrfuss, J., Brass, M., Neumann, J., & von Cramon, D.Y. (2005). Involvement of the inferior frontal junction in cognitive control: Meta-analyses of switching and Stroop studies. *Human Brain Mapping, 25*, 22-34.
- 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.
- DeSouza, J.F., Menon, R.S., & Everling, S. (2003). Preparatory set Associated with pro-saccades and anti-saccades in humans investigated with event-related fMRI. *Journal of Neurophysiology, 89*, 1016-1023.
- Diamond, A. (2013). Executive functions. *Annual Review of Psychology, 64*, 135-168.
- Dinoff, A., Herrmann, N., Swardfager, W., & Lanctôt, K.L. (2017). The effect of acute exercise on blood concentrations of brain-derived neurotrophic factor in healthy adults: a meta-analysis. *European Journal of Neuroscience, 46*, 1635-1646.
- Donchin, E., & Coles, M.G. (1988). Is the P300 component a manifestation of context updating? *Behavioral and Brain Sciences, 11*, 357-374.
- Edelman, J.A., & Goldberg, M.E. (2001). Dependence of saccade-related activity in the primate superior colliculus on visual target presence. *Journal of Neurophysiology, 86*, 676-691.
- Etnier, J.L., Nowell, P.M., Landers, D.M., & Sibley, B.A. (2006). A meta-regression to examine the relationship between aerobic fitness and cognitive performance. *Brain Research Reviews, 52*, 119-130.



- Everling, S., & Johnston, K. (2013). Control of the superior colliculus by the lateral prefrontal cortex. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *368*, 20130068.
- Fischer, B., & Weber, H. (1992). Characteristics of “anti” saccades in man. *Experimental Brain Research*, *89*, 415-424.
- Fitts, P.M. (1954). The information capacity of the human motor system in controlling the amplitude of movement. *Journal of Experimental Psychology*, *47*, 381.
- Gillen, C., & Heath, M. (2014). Target frequency influences antisaccade endpoint bias: evidence for perceptual averaging. *Vision Research*, *105*, 151-158.
- Gillen, C., Weiler, J., & Heath, M. (2013). Stimulus-driven saccades are characterized by an invariant undershooting bias: no evidence for a range effect. *Experimental Brain Research*, *230*, 165-174.
- Godin, G. (2011). The Godin-Shephard leisure-time physical activity questionnaire. *The Health and Fitness Journal of Canada*, *4*, 18-22.
- Hallett, P.E. (1978). Primary and secondary saccades to goals defined by instructions. *Vision Research*, *18*, 1279-1296.
- Heath, M., Gillen, C., & Samani, A. (2016). Alternating between pro-and antisaccades: switch-costs manifest via decoupling the spatial relations between stimulus and response. *Experimental Brain Research*, *234*, 853-865.
- Heath, M., Gillen, C., & Weiler, J. (2015). The antisaccade task: vector inversion contributes to a statistical summary representation of target eccentricities. *Journal of Vision*, *15*, 4-4.
- 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.
- Heath, M., Weiler, J., Marriott, K., & Welsh, T.N. (2011). Vector inversion diminishes the online control of antisaccades. *Experimental Brain Research*, *209*, 117-127.
- Hillman, C.H., Kramer, A.F., Belopolsky, A.V., & Smith, D.P. (2006). A cross-sectional examination of age and physical activity on performance and event-related brain potentials in a task switching paradigm. *International Journal of Psychophysiology*, *59*, 30-39.
- Hillman, C.H., Snook, E.M., & Jerome, G.J. (2003). Acute cardiovascular exercise and executive control function. *International Journal of Psychophysiology*, *48*, 307-314.

- Johnson, L., Addamo, P.K., Raj, I.S., Borkoles, E., Wyckelsma, V., Cyarto, E., & Polman, R.C. (2016). An acute bout of exercise improves the cognitive performance of older adults. *Journal of Aging and Physical Activity*, *24*, 591-598.
- Kamijo, K., & Takeda, Y. (2010). Regular physical activity improves executive function during task switching in young adults. *International Journal of Psychophysiology*, *75*, 304-311.
- Kleiner, M., Brainard, D., & Pelli, D. (2007). What's new in Psychtoolbox-3? *Perception*, *36*, ECVF Abstract Supplement.
- Knaepen, K., Goekint, M., Heyman, E.M., & Meeusen, R. (2010). Neuroplasticity—exercise-induced response of peripheral brain-derived neurotrophic factor. *Sports Medicine*, *40*, 765–801.
- Kramer, A.F., Hahn, S., Cohen, N.J., Banich, M.T., McAuley, E., Harrison, C.R., ... & Colcombe, A. (1999). Ageing, fitness and neurocognitive function. *Nature*, *400*, 418.
- Kubesch, S., Bretschneider, V., Freudemann, R., Weidenhammer, N., Lehmann, M., Spitzer, M., & Gron, G. (2003). Aerobic endurance exercise improves executive functions in depressed patients. *Journal of Clinical Psychiatry*, *64*, 1005-1012.
- Lambourne, K., & Tomporowski, P. (2010). The effect of exercise-induced arousal on cognitive task performance: a meta-regression analysis. *Brain Research*, *1341*, 12–24.
- Leckie, R.L., Oberlin, L.E., Voss, M.W., Prakash, R.S., Szabo-Reed, A., Chaddock-Heyman, L., ... & Martin, S.A. (2014). BDNF mediates improvements in executive function following a 1-year exercise intervention. *Frontiers in Human Neuroscience*, *8*, 985.
- Li, L., Wang, M., Zhao, Q.J., & Fogelson, N. (2012). Neural mechanisms underlying the cost of task switching: an ERP study. *PLoS One*, *7*, e42233.
- Loftus, G.R., & Masson, M.E. (1994). Using confidence intervals in within-subject designs. *Psychonomic Bulletin and Review*, *1*, 476-490.
- 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*, 1611-1626.
- Moore, C.I., & Cao, R. (2008). The hemo-neural hypothesis: on the role of blood flow in information processing. *Journal of Neurophysiology*, *99*, 2035-2047.
- Munoz, D.P., & Everling, S. (2004). Look away: the anti-saccade task and the voluntary control of eye movements. *Nature Reviews Neuroscience*, *5*, 218-228.

- Nee, D.E., Wager, T.D., & Jonides, J. (2007). Interference resolution: insights from a meta-analysis of neuroimaging tasks. *Cognitive, Affective, and Behavioral Neuroscience*, 7, 1-17.
- Nowrangi, M.A., Lyketsos, C., Rao, V., & Munro, C.A. (2014). Systematic review of neuroimaging correlates of executive functioning: converging evidence from different clinical populations. *The Journal of Neuropsychiatry and Clinical Neurosciences*, 26, 114-125.
- Ogoh, S., & Ainslie, P.N. (2009). Regulatory mechanisms of cerebral blood flow during exercise: new concepts. *Exercise and Sport Sciences Reviews*, 37, 123-129.
- 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.
- Pierrot-Deseilligny, C. H., Rivaud, S., Gaymard, B., & Agid, Y. (1991). Cortical control of reflexive visually-guided saccades. *Brain*, 114, 1473-1485.
- Pierrot-Deseilligny, C., Rivaud, S., Gaymard, B., Müri, R., & Vermersch, A.I. (1995). Cortical control of saccades. *Annals of Neurology*, 37, 557-567.
- Schmitter-Edgecombe, M., & Sanders, C. (2009). Task switching in mild cognitive impairment: switch and nonswitch costs. *Journal of the International Neuropsychological Society*, 15, 103-111.
- Scudder, M.R., Drollette, E.S., Pontifex, M.B., & Hillman, C.H. (2012). Neuroelectric indices of goal maintenance following a single bout of physical activity. *Biological Psychology*, 89, 528-531.
- Tari, B., Fadel, M.A., & Heath, M. (2019). Response suppression produces a switch-cost for spatially compatible saccades. *Experimental Brain Research*, 237, 1195-1203.
- Tomporowski, P.D., Davis, C.L., Lambourne, K., Gregoski, M., & Tkacz, J. (2008). Task switching in overweight children: effects of acute exercise and age. *Journal of Sport and Exercise Psychology*, 30, 497-511.
- Tomporowski, P.D., & Ganio, M.S. (2006). Short-term effects of aerobic exercise on executive processing, memory, and emotional reactivity. *International Journal of Sport and Exercise Psychology*, 4, 57-72.
- Tsai, C.L., Pan, C.Y., Chen, F.C., Wang, C.H., & Chou, F.Y. (2016). Effects of acute aerobic exercise on a task-switching protocol and brain-derived neurotrophic factor concentrations in young adults with different levels of cardiorespiratory fitness. *Experimental Physiology*, 101, 836-850.

- United States, Department of Health, and Human Services, 1996. Physical activity and health: a report of the surgeon general. Diane Publishing, Atlanta, GA.
- Weiler, J., Hassall, C.D., Krigolson, O.E., & Heath, M. (2015). The unidirectional prosaccade switch-cost: electroencephalographic evidence of task-set inertia in oculomotor control. *Behavioural Brain Research*, 278, 323-329.
- Weiler, J., & Heath, M. (2012a). The prior-antisaccade effect influences the planning and online control of prosaccades. *Experimental Brain Research*, 216, 545-552.
- Weiler, J., & Heath, M. (2012b). Task-switching in oculomotor control: unidirectional switch-cost when alternating between pro-and antisaccades. *Neuroscience Letters*, 530, 150-154.
- Weiler, J., & Heath, M. (2014a). Oculomotor task switching: alternating from a nonstandard to a standard response yields the unidirectional prosaccade switch-cost. *Journal of Neurophysiology*, 112, 2176–2184.
- Weiler, J., & Heath, M. (2014b). Repetitive antisaccade execution does not increase the unidirectional prosaccade switch-cost. *Acta Psychologica*, 146, 67-72.
- Weiler, J., Mitchell, T., & Heath, M. (2014). Response suppression delays the planning of subsequent stimulus-driven saccades. *PLoS One*, 9, e86408.
- Winter, B., Breitenstein, C., Mooren, F.C., Voelker, K., Fobker, M., Lechtermann, A., ... & Knecht, S. (2007). High impact running improves learning. *Neurobiology of Learning and Memory*, 87, 597-609.
- Wurtz, R.H., & Albano, J.E. (1980). Visual-motor function of the primate superior colliculus. *Annual Review of Neuroscience*, 3, 189-226.
- Wylie, G., & Allport, A. (2000). Task switching and the measurement of “switch costs”. *Psychological Research*, 63, 212-233.
- Yanagisawa, H., Dan, I., Tsuzuki, D., Kato, M., Okamoto, M., Kyutoku, Y., & Soya, H. (2010). Acute moderate exercise elicits increased dorsolateral prefrontal activation and improves cognitive performance with Stroop test. *NeuroImage*, 50, 1702-1710.
- Yeung, N., Nystrom, L.E., Aronson, J.A., & Cohen, J.D. (2006). Between-task competition and cognitive control in task switching. *Journal of Neuroscience*, 26, 1429-1438.

## Chapter 3

A single bout of aerobic exercise provides an immediate and longer-term benefit to cognitive flexibility: Evidence from oculomotor task-switching

### 3.1 Introduction

A wealth of evidence has shown that a single bout of aerobic exercise provides a short-term ‘boost’ to executive function (for meta analyses see Chang, Labban, Gapin, & Etnier, 2012; Lambourne & Tomporowski, 2010; Ludyga, Gerber, Brand, Holsboer-Trachsler, & Pühse, 2016). Executive function refers to the multi-dimensional components of inhibitory control, working memory, and cognitive flexibility (Diamond, 2013) with each being critical to successful activities of daily living. Notably, work demonstrating a single bout of exercise benefit to executive function has largely focused on inhibitory control and working memory tasks (for meta-analyses see Chang et al., 2012; Lambourne & Tomporowski, 2010; Ludyga et al., 2016). For example, Chu and colleagues (Chu, Alderman, Wei, & Chang, 2015) showed that following 30-min of acute exercise (via cycle ergometer) at a moderate intensity (60-70% of age-predicted maximum heart rate [ $HR_{max}$ ]) healthy young participants exhibited improved performance on the stop-signal task (SST). In turn, Li et al. (2014) had participants exercise for 20-min (via cycle ergometer at 60-70% of  $HR_{max}$ ) and examined concurrent behavioural and functional magnetic resonance imaging (fMRI) measures of the n-back task pre- and post-exercise. Results showed improved post-exercise n-back performance and was a result linked to a task-dependent increase in activity within the frontoparietal networks known to mediate executive function. The proposed neurobiological mechanisms associated with the post-exercise improvement to inhibitory control and working memory include: (1) increased brain derived neurotrophic factor (BDNF) (Dinoff, Herrmann, Swardfager, & Lanctôt, 2017) and/or catecholamine concentration (Winter et al., 2007), and (2) increased regional cerebral blood flow (CBF) (Hiura, Mizuno, & Fujimoto, 2010; Seifert & Secher, 2011; Verburch, Königs, Scherder, & Oosterlaan, 2014) that leads to temperature- and mechanical-based changes to brain’s neural networks and glial networks that improve information processing (Moore & Cao, 2008).

From the above it is clear that the inhibitory control and working memory components of executive function benefit from a single bout of exercise. It is, however, less clear whether cognitive flexibility demonstrates a similar benefit. This is a salient issue as there is continued debate as to whether executive function represents a unitary or dissociable construct (Best & Miller, 2010). Cognitive flexibility reflects our ability to alternate between different attentional- and motor-related goals to account for dynamic changes to our environment and is an executive

component typically examined via a task-switching paradigm (Diamond, 2013). In a task-switching paradigm, participants alternate between different tasks after every second trial (i.e., AABB) and the resultant ‘switch’ has been found to increase RTs and/or response errors (i.e., a switch-cost) (Allport, Styles, & Hsieh, 1994; Tsai, Pan, Chen, Wang, & Chou, 2016). In the exercise neuroscience literature, there are a paucity of studies examining the impact of an acute bout of exercise on cognitive flexibility and the results of this work are mixed. For example, Bae and Masaki (2019) had young adults complete 30-min of acute aerobic exercise (via treadmill) at 70%  $HR_{max}$  and assessed cognitive flexibility pre- and post-exercise using a task-switching paradigm wherein participants alternated between parity (i.e., odd/even) and size (i.e., low/high) judgement tasks (A=parity; B=size) (see also Tsai et al., 2016). The authors reported shorter RTs on task-switch trials post-exercise – a result suggesting that a single bout of exercise facilitates cognitive flexibility. In contrast, Tomporowski & Ganio (2006) investigated whether 40-min of aerobic exercise (via cycling ergometer) at 60% of  $VO_{2max}$  improved young adults’ ability to switch between odd/even and vowel/consonant judgement task in an AABB paradigm. The authors reported that acute exercise did not facilitate task-switching efficiency. One interpretation for the equivocal findings is that cognitive flexibility is mediated via a distinct executive circuitry that is refractory or sensitive to only subtle changes in neural efficiency following a single bout of exercise (for review, see Logue & Gould, 2014). Such an interpretation would be in line with lesion and neuropsychiatric studies reporting that the core components of executive function are interconnected but independent processes (Gilbert & Burgess, 2008; Thoma et al., 2007). More notably, I believe that the equivocal findings relate to previous task-switching studies including non-executive components (i.e., numerosity, parity, language processing) that do not provide the resolution to detect subtle executive benefits. In support of that view, Chapter Two of my thesis showed that a single bout of moderate-to-heavy intensity aerobic exercise (via cycle ergometer at 80% of  $HR_{max}$ ) improved task-switching efficiency immediately (i.e., 0-17-min) post-exercise using pro- and antisaccades in an AABB task-switching paradigm. Accordingly, I believe it is necessary to employ a task independent of non-executive cognitive processes to adequately examine the positive post-exercise benefits to cognitive flexibility.

A question arising from Chapter Two relates to the period of time a post-exercise benefit to cognitive flexibility persists. Lambourne and Tomporowski’s (2010) meta-analysis reported

that exercise-induced benefit to executive function persists for up to 15-min post-exercise, whereas Chang et al.'s (2012) meta-analysis concluded that the largest and most reliable exercise benefit to executive function occurs 11-20-min post-exercise and this benefit subsides following a longer (i.e., >20-min) delay. More notably, the limited research focusing on the time course effects of a single bout of exercise has exclusively focused on inhibitory control tasks and has produced equivocal results. For example, Joyce and colleagues examined the time course effects by employing the inhibitory control stop-signal task (SST) during exercise and immediately, and 30-min following an acute aerobic exercise (i.e., for 30-min via cycle ergometer at 40% of maximal aerobic power). Results showed a post-exercise benefit that persisted up to 52-min post-exercise. In contrast, Barella et al. (2010) recruited healthy older adults to study the immediate and delayed (i.e., 5, 10, 15, 20, 30, 45, 60, 75, 90, 105, 120 min post-exercise) effects of acute aerobic exercise (i.e., at  $60\% \pm 3\%$  of heart rate reserve for 20-min via treadmill) on inhibitory control using the Stroop task. Barella et al. reported a post-exercise improvement to information processing with shorter RTs for Stroop colour task (i.e., orally identified the colour of a circle "O" stimulus) for up to 60-min post-exercise, whereas there was no improvement in RTs for the Stroop interference or inhibition tests post-exercise. In other words, Barella et al. reported a benefit for information processing but not for executive function. To my knowledge, no previous studies have examined a post-exercise benefits to cognitive flexibility beyond the immediate assessment protocol used in Chapter Two. This is an important issue because the distinct neural circuitry of cognitive flexibility may not follow the same time course effects as the other core components of executive function. Accordingly, the goal of Chapter Three was to examine for how long a 20-min bout of acute aerobic exercise (via cycle ergometer at 80% of  $HR_{max}$ ) benefits cognitive flexibility.

The present work examined post-exercise cognitive flexibility via a paradigm similar to Chapter Two with two notable exceptions. First, I examined a post-exercise benefit to cognitive flexibility immediately, 30- and 60-min post-exercise. As indicated above, the inclusion of the multiple post-exercise assessments was used to determine for how long a benefit persists. Second, instead of pro- and antisaccades, the present work involved stimulus-driven (SD) and minimally delayed (MD) saccades arranged in an AABB paradigm. SD saccades are a standard task requiring a response *at* target onset (i.e., they represent the prosaccade paradigm used in Chapter 2) and are mediated via direct retinotopic maps within the superior colliculus (SC) that



require minimal executive control for their evocation (Wurtz & Albano, 1980). In contrast, MD saccades are a non-standard task requiring the suppression of a pre-potent SD saccade and the initiation of a response *after* target offset. MD saccades therefore require response suppression without the need for vector inversion included in the antisaccade (see Chapter Two). Notably, most recent work by my group has shown that the SD and MD saccade paradigm produces a switch-cost magnitude larger than that associated with pro- and antisaccades. For example, Tari et al. showed that SD and MD saccades in an AABB paradigm result in a large magnitude ( $d_z > 1.5$ ) *unidirectional switch-cost* (Tari, Fadel, & Heath, 2019; Tari & Heath, 2019) wherein a SD saccade preceded by a MD saccade (i.e., task-switch trial) produce a 25-30 ms increase in reaction time (RT) compared to a SD saccade preceded its same task-type (i.e., task-repeat trial). In turn, RTs do not reliably differ for MD task-switch and task-repeat trials. As indicated by Davranche and Audiffren (2004) the application of a task producing the largest magnitude difference between tasks is optimal for research examining subtle post-exercise changes in executive function.

As outlined above, no work has examined for how long a single bout of exercise benefits cognitive flexibility. Accordingly, I employed a SD and MD task-switching paradigm during separate assessments that occurred pre-exercise and immediate, 30- and 60-min post-exercise. The inclusion of 30-min post-exercise assessment was based on previous work involving inhibitory control tasks. The 60-min post-exercise assessment was used because previous work has suggested that elevated peripheral brain-derived neurotrophic factor (BDNF) concentration (Knaepen et al., 2010) as well as increased cerebral blood flow (Halliwill, 2001) are present within this window. In terms of research predictions, a post-exercise improvement in cognitive flexibility should manifest via a reduced magnitude unidirectional switch-cost compared to the pre-exercise assessment. Further, if a single bout of exercise provides more than a transient ‘boost’ to cognitive flexibility then the reduced switch-cost magnitude should be observed not only immediately post-exercise but also across the 30- and 60-min intervals.

## 3.2 Methods

### *Participants*

The sample size of 20 participants was based on a power level of .80 (alpha = .05, two-tailed) with a standard deviation and effect size estimate derived from an earlier study by our group (Samani & Heath, 2018). Twenty participants (11 female and 9 male; age range 18-28 years) from the University of Western Ontario community volunteered for this study. The inclusion and exclusion criteria used here mirror those of Chapter Two. All participants obtained a full score on the Physical Activity Readiness Questionnaire (PAR-Q) and achieved a group mean score of 57 (SD=19; Range=30-98) on the Godin Leisure-Time Exercise Questionnaire (GLEETQ) indicating that participants were 'recreationally active' (Amireault, Godin, Lacombe, & Sabiston, 2015).

Participants refrained from strenuous exercise, alcohol and caffeine consumption 12 hr prior to the protocol, and were encouraged to get eight hours of sleep the night before data collection. All participants signed a consent form approved by the Health Sciences Research Ethics Board, University of Western Ontario, and this study was conducted in accordance with the Declaration of Helsinki.

#### *Exercise Intervention*

The exercise equipment and intervention used in Chapter Two was used here.

#### *Oculomotor Task*

Four oculomotor assessments were used (**Figure 6b**). For each assessment, participants sat on a height adjustable chair in front of a tabletop (760 mm in height) with their head placed in a head-chin rest. A 30-inch LCD monitor (60 Hz, 8 ms response rate, 1280 x 960 pixels; Dell 3007WFP, Round Rock, TX, USA) presented visual stimuli and was located at participants' midline and 550 mm from the front edge of the table. The gaze position of participants' left eye was measured via a video-based eye-tracking system (EyeLink 1000 Plus, SR Research, Ottawa, ON, Canada) sampling at 1000 Hz. A nine-point calibration of the viewing space was performed prior to data collection and was confirmed via a follow-up validation (i.e.,  $<1^\circ$  of error for each point in the calibration grid). Computer events were controlled via MATLAB (R2018b, The MathWorks, Natick, MA, USA) and the Psychophysics Toolbox extensions (v 3.0) (Brainard, 1997; Kleiner, Brainard, & Pelli, 2007) including the EyeLink Toolbox (Cornelissen, Peters, & Palmer, 2002). The lights in the experimental suite were extinguished during data collection.

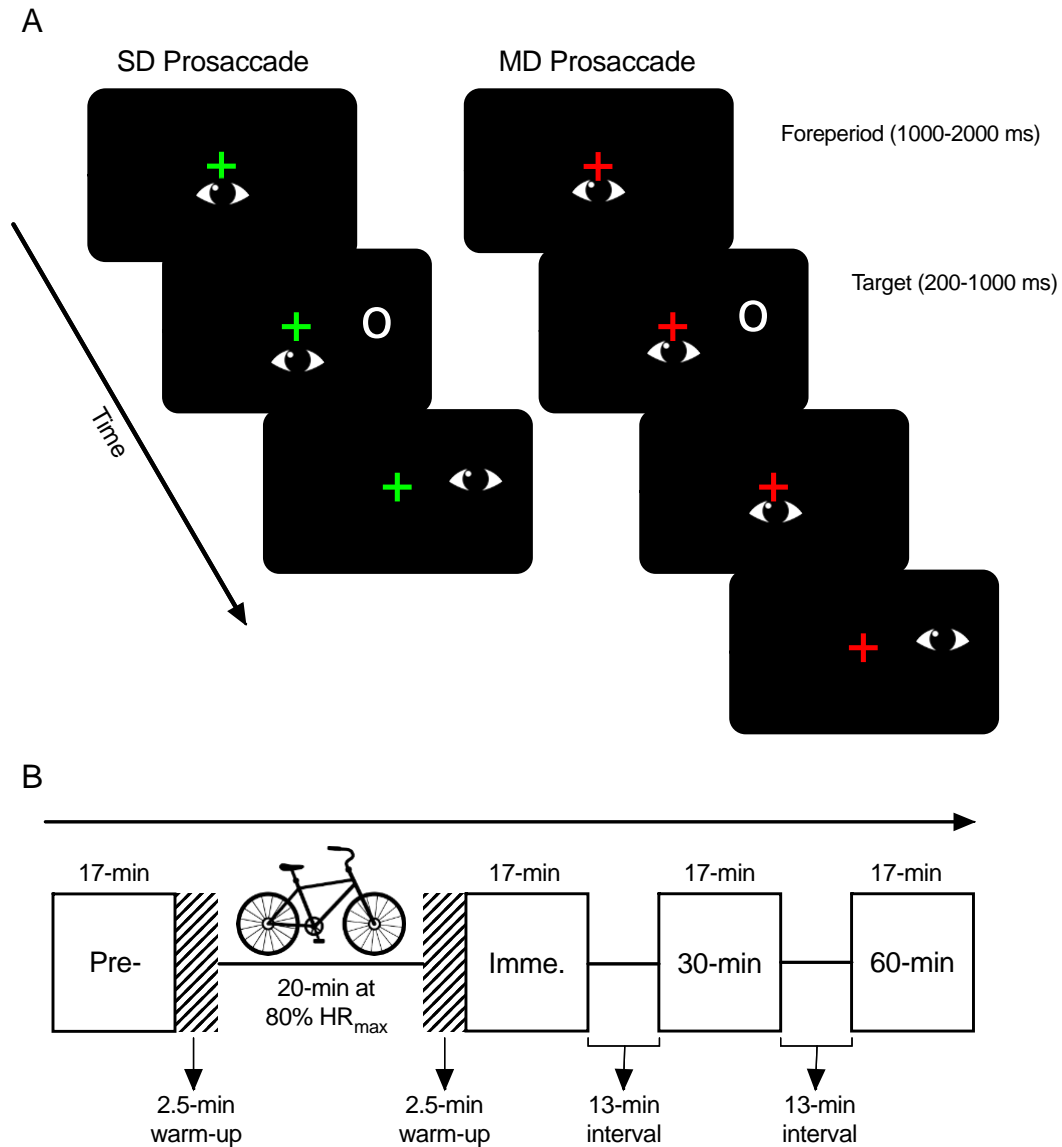
Visual stimuli were presented on a black screen (0.1 cd/m<sup>2</sup>) and included a luminance matched central fixation cross (1.0°, 42 cd/m<sup>2</sup>) that appeared as green or red, and open white

target circles (163 cd/m<sup>2</sup>: 2.5° in diameter) 13.5° (i.e., proximal) and 17.5° (i.e., distal) to the left and right of the fixation cross and in the same horizontal meridian. The fixation cross colour indicated the nature of an upcoming trial. For one half of the participants, a green fixation cross indicated a saccade to veridical target location *at* target onset (i.e., stimulus-driven saccade: SD), whereas the red fixation cross indicated a saccade to veridical target location *after* it was extinguished (i.e., minimally delayed saccade: MD). Thus, MD saccades required active inhibition of a pre-potent SD saccade and is a task-type requiring top-down executive control (Knox, De-Allie, & Wolohan, 2018; Wolohan & Knox, 2014). For the other half of participants, the converse fixation-colour and task-type mapping was used. **Figure 6a** presents the timeline of visual and motor events for SD and MD saccades. For each trial, the fixation cross was presented, and after participants achieved a stable gaze (i.e.,  $\pm 1.5^\circ$  for 450 ms), a uniformly distributed randomized foreperiod (1000-2000 ms) was initiated after which a target was presented. The target was presented for a uniformly distributed period between 200 and 1000 ms whereupon it was extinguished, and the fixation cross remained visible throughout a trial (i.e., overlap paradigm). The target presentation interval was based on Knox et al.'s (2018) work showing that such an interval results in longer RTs for MD than SD saccades (see also Tari et al., 2019; Tari & Heath, 2019).

Each oculomotor assessment included a single block of 160 SD and MD saccades alternated after every second trial (i.e., AABB: A=SD, B=MD). In particular, trials were equally divided into 80 task-repeat (e.g., SD or MD saccade preceded by its same task counterpart) and 80 task-switch (e.g., SD saccade preceded by a MD saccade or vice versa) trials. The ordering of target location (i.e., left and right; proximal and distal) was pseudo-randomized in one of four pre-determined trial sequences. The first trial was counterbalanced for task-type (i.e., SD or MD) and was excluded from data analyses because it was neither a task-switch nor a task-repeat saccade.

**Figure 6b** shows the timeline of each oculomotor assessment. Once the pre-exercise assessment was completed participants commenced the exercise intervention. When the cool-down period (2.5-min) associated with the exercise intervention was concluded the immediate post-exercise assessment was started. In turn, **Figure 6b** shows that additional assessments were completed at 30- and 60-min intervals following commencement of the immediate post-exercise assessment. Each oculomotor assessment required approximately 17-min to complete. As such,

and as demonstrated in **Figure 6b**, the immediate, 30- and 60-min post-exercise assessments provided intervals to assess task-switching efficiency within windows of 0-17 min, 30-47, and 60-77 min post-exercise, respectively.



**Figure 6.** Panel A provides a schematic of visual event for stimulus-driven and minimally delayed saccades. The green fixation cross cued a saccade immediately to a target’s veridical location (i.e., stimulus-driven prosaccade), whereas the red fixation cross cued a saccade at target offset (i.e., minimally delayed prosaccade). Notably, the schematic shows only a single target eccentricity to the right of fixation; however, in the task-switching block the target eccentricity (i.e., 13.5° and 17.5°) and target location (i.e., left and right of fixation) were pseudo-randomized.

Panel B shows the timeline of four oculomotor assessments including pre-exercise (Pre-), immediate (Imme.), 30-, and 60-min post-exercise assessments in relation to the timing of the exercise protocol.

#### *Data reduction, dependent variables, and statistical analysis*

Data reduction and dependent variables were the same as Chapter Two. We note that trials involving a signal loss accounted for less than 1% of trials and less than 11% of trials were removed due to the outlier criterion specified in Chapter Two.

Dependent variables were analyzed via 4 (time: pre-exercise, immediately post-exercise, 30-min post-exercise, 60 min post-exercise) by 2 (task: SD, MD) by 2 (task-transition: task-switch, task-repeat) fully repeated measures ANOVA. Simple effects contrasts were used for post hoc analyses.

### 3.3 Results

#### *Exemplar participant: SD and MD trajectories*

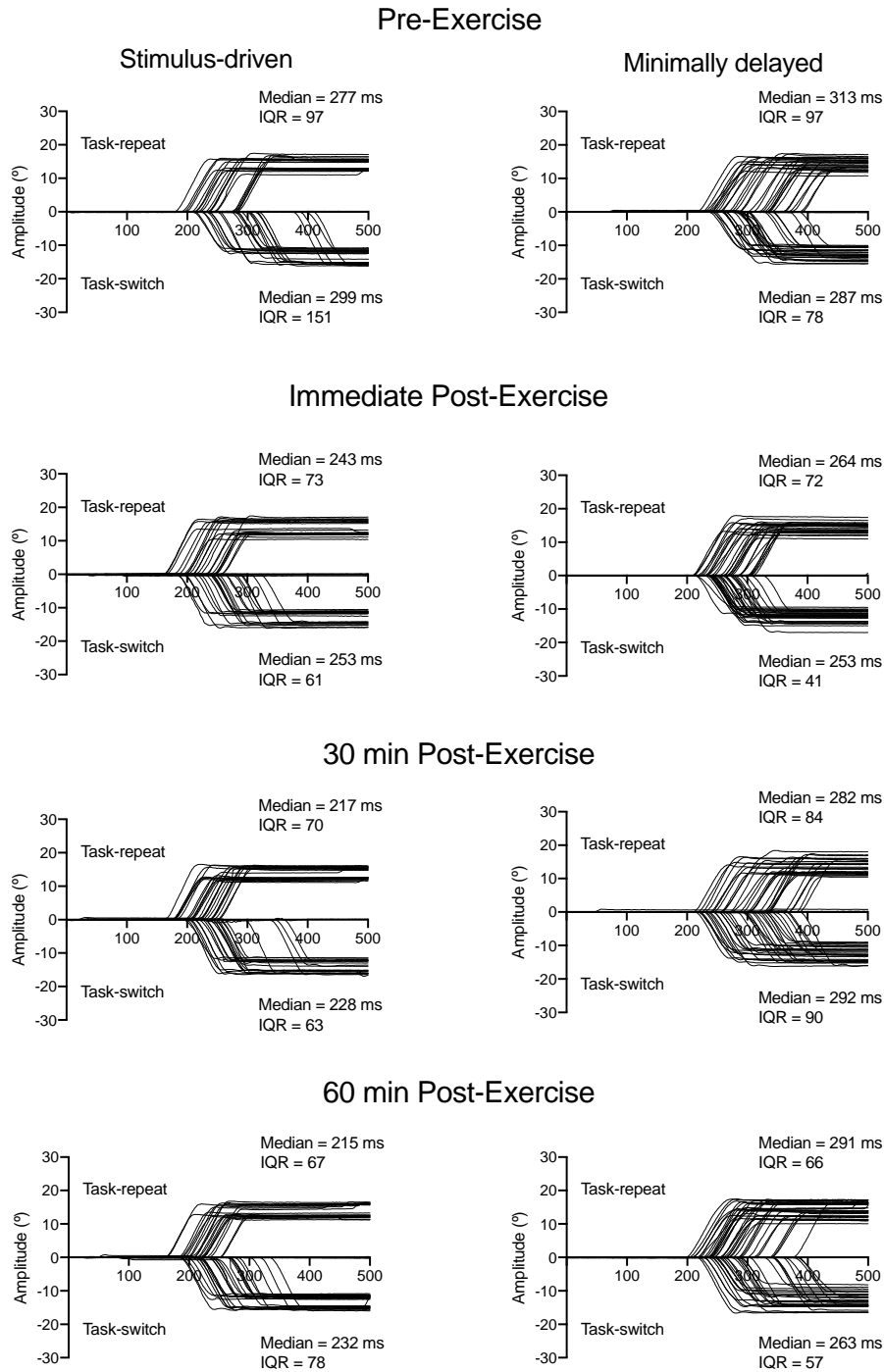
**Figure 7** shows an exemplar participant's position by time trajectories for SD and MD task-switch and task-repeat trials at pre- and immediate, 30- and 60-min post-exercise assessments. The figure demonstrates that RTs for SD task-repeat trials were shorter and less variable than their task-switch counterparts, whereas MD task-switch and task-repeat trials were comparable. More notably, the figure demonstrates that the magnitude of the difference between SD task-switch and task-repeat trials was larger during the pre-exercise and the 60-min post-exercise assessments as compared to the immediate and 30-minute post-exercise assessments.

#### *Reaction time*

**Figure 8** shows RT percent frequency histograms for SD and MD task-switch and task-repeat saccades at pre-, immediate, 30- and 60-min post-exercise assessments. The figure qualitatively demonstrates that RTs for SD task-repeat saccades were shorter and less variable than their task-switch counterparts and that this difference was larger at the pre- and 60-min assessments. In turn, RTs for MD task-switch and task-repeat saccades did not differ. The histograms also that SD and MD saccades produced an equivalent frequency of anticipatory responses, whereas SD saccades demonstrated a greater frequency of short-latency responses.

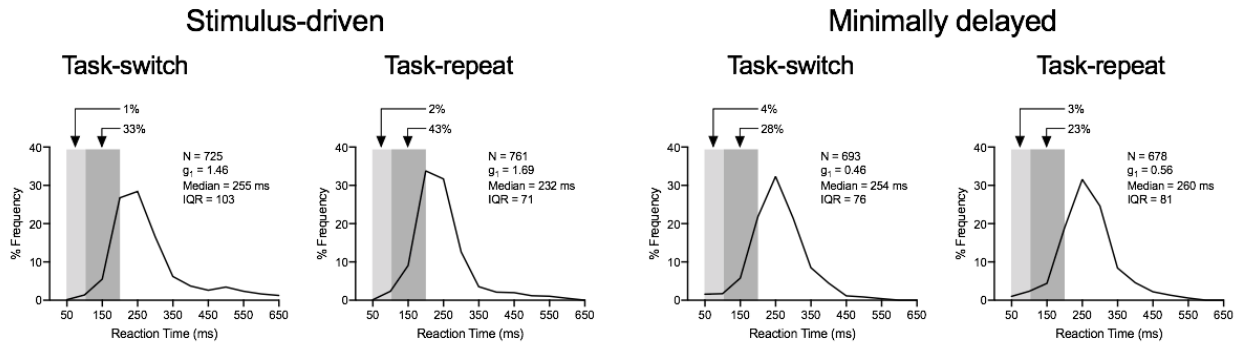
Notably, however, the percentage of anticipatory and short-latency saccades did not differ across pre- to each post-exercise oculomotor assessments. In terms of quantitative analyses, RT produced main effects for time,  $F(3,57)=13.77$ ,  $p<.001$ ,  $\eta_p^2=.42$ , task,  $F(1,19)=9.25$ ,  $p<.01$ ,  $\eta_p^2=.33$ , task-transition,  $F(1,19)=13.62$ ,  $p<.01$ ,  $\eta_p^2=.42$ , and interactions involving task by task-transition,  $F(1,19)=30.56$ ,  $p<.001$ ,  $\eta_p^2=.62$ , and time by task by task-transition,  $F(3,57)=3.13$ ,  $p=.03$ ,  $\eta_p^2=.14$ . **Figure 9a** shows that RTs for SD task-switch saccades were longer than their task-repeat counterparts at each assessment (all  $t(19)=6.14$ , 3.60, 3.30 and 7.75, for the pre-, immediate, 30-, and 60-min assessments, respectively,  $ps<.01$ ), whereas MD task-switch and task-repeat saccades did not reliably differ at any assessment (all  $t(19)<-1.02$ , -0.36, -1.25 and -1.40,  $ps>.18$ ). Accordingly, my post-hoc contrasts did not uncover the nature of the time by task by task-transition interaction. To further address the interaction, I computed participant-specific RT difference scores (i.e., task-switch minus task-repeat) to for SD saccades to determine if the *magnitude* of the switch-cost varied across the different assessments. **Figure 9b** shows that switch-cost at the pre-exercise assessment (23 ms,  $SD=17$ ) was larger than the immediate post-exercise assessment (12 ms,  $SD=15$ ), ( $t(19)=4.10$ ,  $p<.01$ ), which, in turn, did not reliably differ from the 30-min post-exercise assessment (12 ms,  $SD=16$ ) ( $t(19)=-.07$ ,  $p=.95$ ). The switch-cost at the 30-min post-exercise assessment was less than the 60-min post-exercise assessment (21 ms,  $SD=16$ ) ( $t(19)=-2.60$ ,  $p=.02$ ).

Two one-sided test (TOST) statistics (see Lakens, 2017) comparing immediate and 30-min post-exercise assessments ( $t(19)=3.18$ ,  $p=.002$ ), and pre- and 60-min post-exercise assessments ( $t(19)=2.91$ ,  $p=.004$ ) showed that results were within an equivalence boundary. In other words, the immediate and 30-min assessments, but not the pre-exercise and 60-min assessments showed an improvement in task-switching efficiency.

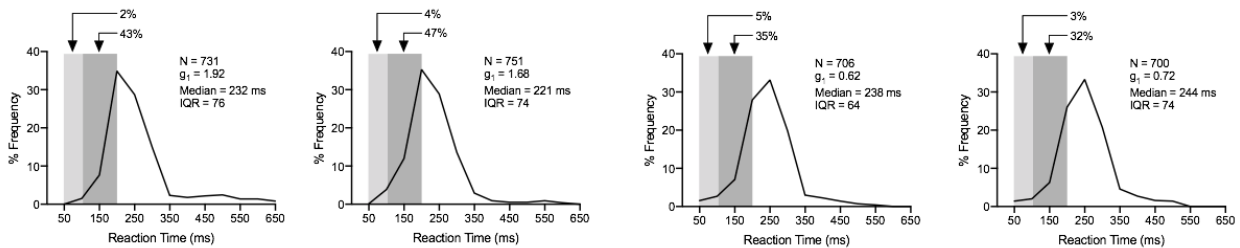


**Figure 7.** Exemplar participant’s trial-to-trial position by time trajectories for stimulus-driven and minimally delayed task-switch and task-repeat saccades at pre-, immediate, 30- and 60-min post-exercise assessments. (Note: time zero represents response cuing). For simplicity, task-switch and task-repeat saccades are depicted as negative and positive trajectory deflections, respectively.

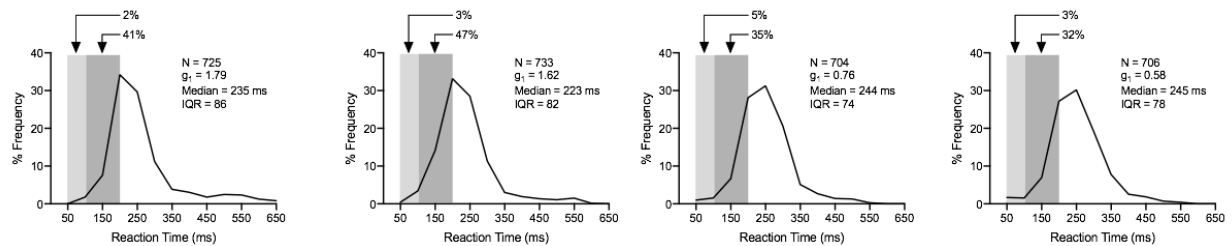
## Pre-Exercise



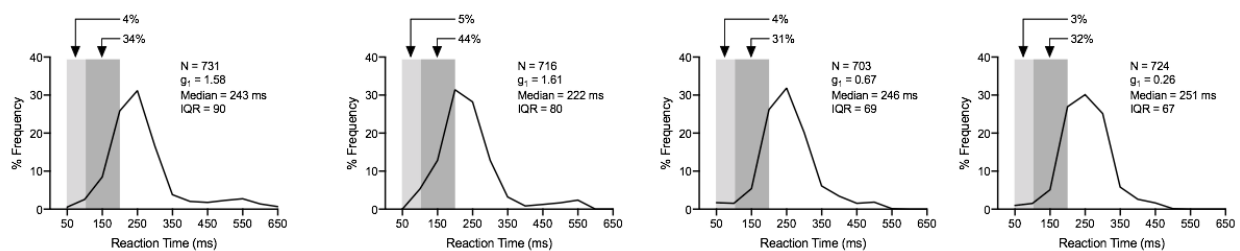
## Immediate Post-Exercise



## 30 min Post-Exercise

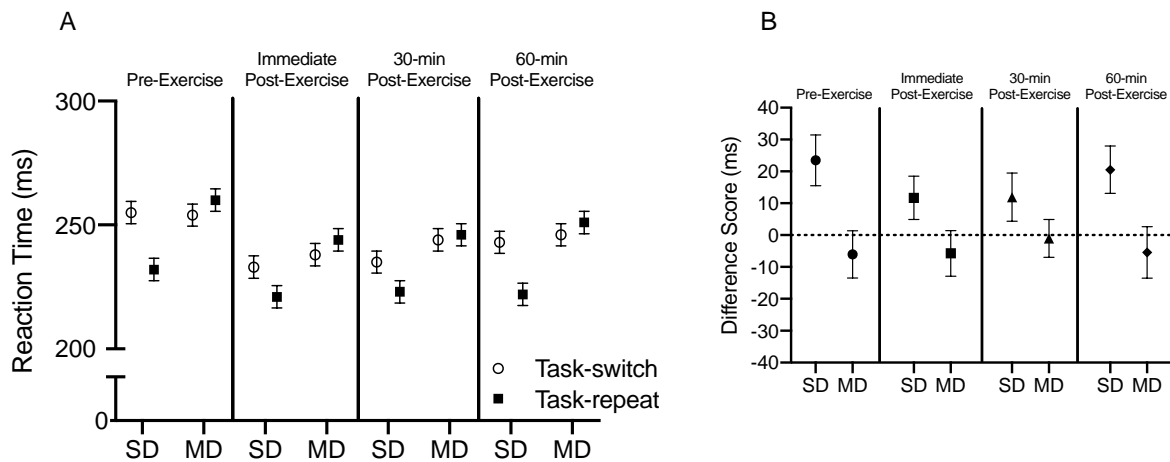


## 60 min Post-Exercise



**Figure 8.** The main panels show reaction time (ms) percent frequency histograms for stimulus-driven and minimally delayed task-switch and task-repeat saccades at pre- and immediate, 30-, and 60-min post-exercise with bin widths of 50 ms. The light and dark grey rectangles in each panel denote anticipatory (<100 ms) and short-latency (100 to <200 ms) responses, respectively.

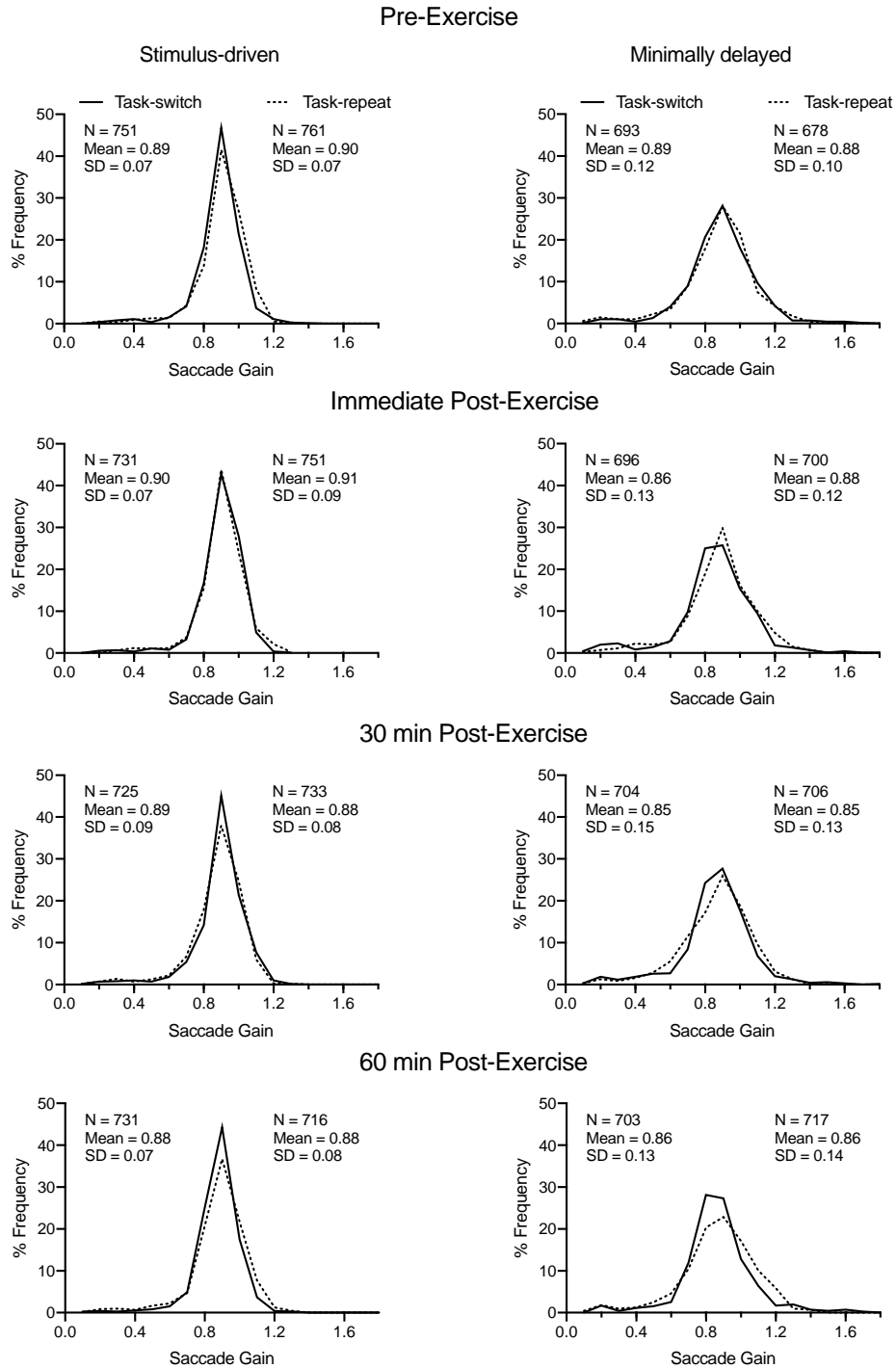




**Figure 9.** The left panel (A) shows group mean stimulus-driven (SD) and minimally delayed (MD) task-switch and task-repeat saccade reaction times (ms) at pre- and each post-exercise assessment. Error bars represent 95% within-participant confidence intervals computed via the mean-squared error term for time by task by task-transition interaction (Loftus & Masson, 1994). The right panel (B) shows group mean SD and MD saccade reaction time difference scores (i.e., task-switch minus task-repeat) at for each assessment. Error bars represent 95% between-participant confidence intervals and the absence of overlap between an error bar and zero (i.e., the horizontal line) represents a reliable effect inclusive to a test of the null hypothesis (Cumming, 2013).

#### *Movement time, saccade gain and gain variability*

Results for MT produced a main effect of task,  $F(1,19)=70.38$ ,  $p<.001$ ,  $\eta_p^2=.79$ : values for SD saccades (54 ms,  $SD=5$ ) were shorter than MD saccades (69 ms,  $SD=10$ ). The main panels of **Figure 10** show gain percent frequency histograms for SD and MD task-switch and task-repeat saccades at pre-, immediate, 30-min and 60-min post-exercise assessments. The figure demonstrates that gains were generally less than unitary (i.e., ~10% undershooting bias) (Harris, 1995). Quantitative analysis showed that saccade gain did not produce any reliable effects or interactions, all  $F(1,19)<2.84$ ,  $ps>.11$ , all  $\eta_p^2<.13$ . Gain variability revealed a main effect for task,  $F(1,19)=29.70$ ,  $p<.001$ ,  $\eta_p^2=.61$ : SD saccades were less variable (0.11,  $SD=0.04$ ) than MD saccades (0.16,  $SD=0.04$ ).



**Figure 10.** The main panels show saccade gain (i.e., saccade amplitude/veridical target location) percent frequency histograms for stimulus-driven (left panels) and minimally delayed (right panels) task-switch and task-repeat saccades at each time of assessment (bin width= 0.1). The textbox within each panel contains the mean and standard deviation for proximal (i.e., 13.5°) and distal (i.e., 17.5°) targets.

### 3.4 Discussion

The goal of the present study was to determine for how long a benefit to cognitive flexibility persists following a single bout of aerobic exercise. To accomplish that goal, I had participants exercise at a moderate-to-heavy intensity for 20-min and SD and MD saccades ordered in an AABB task-switching paradigm were completed prior to exercise and at immediate, 30-, and 60-min post-exercise assessments.

#### *A pre-exercise unidirectional switch-cost*

Knox and colleagues (Knox et al., 2018; Wolohan & Knox, 2014) examined SD and MD saccades in separate blocks and reported longer RTs in the latter condition across a 200 – 1000 ms target delay interval (i.e., the interval as used here). Based on those findings, the authors proposed that MD saccades provide a direct measure of executive control that is less influenced by ‘additional’ cognitive processes (i.e., attention, working memory) than the more frequently used antisaccade task. Additionally, previous work by my group showed that SD and MD saccades ordered in an AABB paradigm result in a *unidirectional switch-cost*. In particular, Tari et al. (2019) reported that RTs for SD task-switch saccades were 25-30 ms longer than their task-repeat counterparts, whereas RTs for MD task-switch and task-repeat trials did not reliably differ (see also Tari & Heath, 2019). In the current work I found that pre-exercise SD task-switch saccades (255 ms, SD=24) produced RTs that were longer than their task-repeat (232 ms, SD=23) counterparts, whereas RTs for MD task-switch (254 ms, SD=27) and task-repeat (260 ms, SD=31) saccades did not reliably differ. In other words, the pre-exercise findings exhibited a 23 ms *unidirectional switch-cost* (Tari et al., 2019; Tari & Heath, 2019; Weiler, Hassall, Krigolson, & Heath, 2015; Weiler & Heath, 2012a, 2012b, 2014a, 2014b; Weiler, Mitchell, & Heath, 2014). In line with my group’s previous work, I have interpreted these results to evince that the top-down task-set necessary to produce a non-standard MD saccade engenders lingering neural activity that proactively delays the planning of a subsequent SD saccade (i.e., the task-set inertia hypothesis) (Allport et al., 1994; Weiler et al., 2015). Most notably, the large magnitude ( $d_z=1.38$ ) unidirectional switch-cost at pre-exercise assessment provides a framework for determining the effect of a single bout of aerobic exercise on task-switching efficiency.

#### *Exercise provides an immediate benefit to cognitive flexibility*

Recall that the immediate post-exercise assessment occurred when participants heart rate was less than 100 bpm and for most participants this occurred within 1-2 min after the cool-down

interval. At this time, results revealed a *unidirectional switch-cost*; however, the switch-cost magnitude (12 ms, SD=15) was less than the pre-exercise assessment (23 ms, SD=17) (see **Figure 8b**). The reduced magnitude switch-cost cannot be attributed to the speed-accuracy trade-off (Fitts, 1954) given that saccade duration and gain variability did not vary from pre- to the immediate post-exercise assessments. Indeed, the only difference associated with the aforementioned metrics was that MD saccades produced longer saccade duration and more variable endpoints than SD saccades – a result attributed to increased level of response and visuomotor uncertainty in the absence of a veridical target (Edelman & Goldberg, 2001). Moreover, it is important to recognize that the reduced magnitude switch-cost aligns with the magnitude of the improved *unidirectional prosaccade switch-cost* observed in Chapter Two. Accordingly, I propose that an oculomotor task-switching paradigm provides the requisite resolution to detect a reliable immediate post-exercise benefit to the cognitive flexibility core component of executive function.

*A benefit to cognitive flexibility persists for upwards of 47-min post-exercise.*

The 30-min post-exercise assessment produced a unidirectional switch-cost (12 ms) equivalent in magnitude to the immediate assessment and was less than that observed at the 60-min assessment (21 ms). More notably, results indicated that switch-cost magnitudes between immediate and 30-min assessments, and between pre-exercise and 60-min assessments were within an equivalence boundary (i.e., TOST statistics). In other words, improved task-switching efficiency was observed at immediate and 30-min assessments – but not for 60-min assessment. Further, in accounting for the assessment-specific changes in RT I note that such findings cannot be attributed to a practice-related improvement in the task-switching paradigm used here given that a reduced magnitude of switch-cost was not present across at the 60-min post-exercise assessment. Moreover, in Chapter Two I showed an immediate reduction in the magnitude of unidirectional prosaccade switch-cost following 20-min of aerobic exercise, however, assessments separated by a 20-min rest interval did not engender a difference in switch-cost magnitude (see also Samani & Heath, 2018). Accordingly, I propose that a single-bout of aerobic exercise benefits task-switching efficiency – and hence cognitive flexibility – for a period not less than 47-min post-exercise. Indeed, as each oculomotor assessment required approximately 17-min to complete (**Figure 6b**), the 47-min interval represents the window of time from onset of the immediate to the completion of the 30-min post-exercise assessments.

I propose that the persistent post-exercise benefit to cognitive flexibility represents improved neural efficiency within the PFC. Support for this view is garnered from neuroimaging, primate, and lesion studies showing that the PFC is fundamentally involved in volitional inhibition (i.e., ability to inhibit goal-directed response) (for review, see Aron, Robbins, & Poldrack, 2004) and evidence demonstrating that a single of aerobic exercise enhances PFC activity (Byun et al., 2014; Yanagisawa et al., 2010). In particular, Moore and Cao's (2008) hemo-neural hypothesis contends that functional hyperemia results in temperature- and mechanical-based changes to local neural networks that enhance neural efficiency and optimize information processing.

#### *Study limitations*

Only healthy young participants were recruited for this study. It is, therefore, unclear whether individuals outside of this age range, and individuals with cognitive impairment, would receive the same temporal 'boost' to cognitive flexibility. This is an important consideration because Tsai et al. (2016) had young adults classified as high- ( $VO_{2max} > 49.2$  ml/kg/min) and low-fit ( $VO_{2max} < 43.1$  ml/kg/min) perform a 30-min single bout of exercise (via treadmill at 60% of  $VO_{2max}$ ). Cognitive flexibility was assessed via AABB task-switching paradigm using parity and size judgement tasks. The authors reported that high-fit – but not low-fit – individuals attained a post-exercise benefit to task-switching efficiency. It is, therefore, possible that the present study observed a reliable post-exercise benefit because only high-fit young individuals were recruited. A second limitation is that although previous work by my group has shown that post-exercise improvement in inhibitory control does not vary across moderate-to-very-heavy intensities (Heath et al., 2018), it is unknown whether a dose-response relationship impacts a post-exercise benefit in cognitive flexibility. Future research should therefore examine whether exercise intensity and/or duration differentially influences the post-exercise improvement in cognitive flexibility.

### **3.5 Conclusions**

A single bout of moderate-to-heavy intensity aerobic exercise resulted in a reliable decrease in the magnitude of a unidirectional switch-cost at an immediate and 30-min post-exercise assessments, whereas no such advantage was observed at 60-min post-exercise assessment. The findings from present study demonstrates that task-switching paradigm

provides a sufficient resolution to detect the subtle changes associated with post-exercise improvement in cognitive flexibility that persist for up to 47-min.

### 3.6 References

- Allport, A., Styles, E.A., & Hsieh, S. (1994). *Shifting intentional set: exploring the dynamic control of tasks*, in: Umiltà, C., Moscovitch, M., (Eds.), *Attention and Performance XV*. MIT Press., Cambridge, pp. 421-452.
- Amireault, S., Godin, G., Lacombe, J., & Sabiston, C.M. (2015). The use of the Godin-Shephard leisure-time physical activity questionnaire in oncology research: a systematic review. *BMC Medical Research Methodology*, 15, 60.
- Aron, A.R., Robbins, T.W., & Poldrack, R.A. (2004). Inhibition and the right inferior frontal cortex. *Trends in Cognitive Sciences*, 8, 170-177.
- Bae, S., & Masaki, H. (2019). Effects of acute aerobic exercise on cognitive flexibility required during task-switching paradigm. *Frontiers in Human Neuroscience*, 13, 260.
- 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, 87-98.
- Best, J.R., & Miller, P.H. (2010). A developmental perspective on executive function. *Child Development*, 81, 1641-1660.
- Brainard, D.H. (1997). The psychophysics toolbox. *Spatial Vision*, 10, 433-436.
- Byun, K., Hyodo, K., Suwabe, K., Ochi, G., Sakairi, Y., Kato, M., ... & Soya, H. (2014). Positive effect of acute mild exercise on executive function via arousal-related prefrontal activations: an fNIRS study. *Neuroimage*, 98, 336-345.
- 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.
- Chu, C.H., Alderman, B.L., Wei, G.X., & Chang, Y.K. (2015). Effects of acute aerobic exercise on motor response inhibition: an ERP study using the stop-signal task. *Journal of Sport and Health Science*, 4, 73-81.
- 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, 613-617.

- Cumming, G. (2013). *Understanding the new statistics: effect sizes, confidence intervals, and meta-analysis*. New York, NY, US: Routledge/Taylor & Francis Group.
- Davranche, K., & Audiffren, M. (2004). Facilitating effects of exercise on information processing. *Journal of Sports Sciences*, *22*, 419-428.
- Diamond, A. (2013). Executive functions. *Annual Review of Psychology*, *64*, 135-168.
- Dinoff, A., Herrmann, N., Swardfager, W., & Lanctôt, K.L. (2017). The effect of acute exercise on blood concentrations of brain-derived neurotrophic factor in healthy adults: a meta-analysis. *European Journal of Neuroscience*, *46*, 1635-1646.
- Edelman, J.A., & Goldberg, M.E. (2001). Dependence of saccade-related activity in the primate superior colliculus on visual target presence. *Journal of Neurophysiology*, *86*, 676-691.
- Fitts, P.M. (1954). The information capacity of the human motor system in controlling the amplitude of movement. *Journal of Experimental Psychology*, *47*, 381.
- Gilbert, S. J., & Burgess, P. W. (2008). Executive function. *Current Biology*, *18*, R110-R114.
- Halliwill, J.R. (2001). Mechanisms and clinical implications of post-exercise hypotension in humans. *Exercise and Sport Sciences Reviews*, *29*, 65-70.
- Harris, C.M. (1995). Does saccadic undershoot minimize saccadic flight-time? A Monte-Carlo study. *Vision Research*, *35*, 691-701.
- 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.
- Hiura, M., Mizuno, T., & Fujimoto, T. (2010). Cerebral oxygenation in the frontal lobe cortex during incremental exercise tests: the regional changes influenced by volitional exhaustion. *Advances in Experimental Medicine and Biology*, *662*, 257-263.
- 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*, 14-19.
- Kleiner, M., Brainard, D., & Pelli, D. (2007). What's new in Psychtoolbox-3? *Perception*, *36*, ECVF Abstract Supplement.
- Knaepen, K., Goekint, M., Heyman, E.M., & Meeusen, R. (2010). Neuroplasticity—exercise-induced response of peripheral brain-derived neurotrophic factor. *Sports Medicine*, *40*, 765-801.

- Knox, P.C., De-Allie, E.H., & Wolohan, F.D. (2018). Probing oculomotor inhibition with the minimally delayed oculomotor response task. *Experimental Brain Research*, 236, 2867-2876.
- Lakens, D. (2017). Equivalence tests: a practical primer for t tests, correlations, and meta-analyses. *Social Psychological and Personality Science*, 8, 355-362.
- Lambourne, K., & Tomporowski, P. (2010). The effect of exercise-induced arousal on cognitive task performance: a meta-regression analysis. *Brain Research*, 1341, 12-24.
- Li, L., Men, W. W., Chang, Y. K., Fan, M. X., Ji, L., & Wei, G. X. (2014). Acute aerobic exercise increases cortical activity during working memory: a functional MRI study in female college students. *PloS One*, 9, e99222.
- Loftus, G.R., & Masson, M.E. (1994). Using confidence intervals in within-subject designs. *Psychonomic Bulletin and Review*, 1, 476-490.
- Logue, S.F., & Gould, T.J. (2014). The neural and genetic basis of executive function: attention, cognitive flexibility, and response inhibition. *Pharmacology Biochemistry and Behavior*, 123, 45-54.
- 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, 1611-1626.
- Moore, C.I., & Cao, R. (2008). The hemo-neural hypothesis: on the role of blood flow in information processing. *Journal of Neurophysiology*, 99, 2035-2047.
- 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.
- Seifert, T., & Secher, N.H. (2011). Sympathetic influence on cerebral blood flow and metabolism during exercise in humans. *Progress in Neurobiology*, 95, 406-426.
- Tari, B., Fadel, M.A., & Heath, M. (2019). Response suppression produces a switch-cost for spatially compatible saccades. *Experimental Brain Research*, 237, 1195-1203.
- Tari, B., & Heath, M. (2019). Pro-and antisaccade task-switching: response suppression—and not vector inversion—contributes to a task-set inertia. *Experimental Brain Research*, 1-10.
- Thoma, P., Wiebel, B., & Daum, I. (2007). Response inhibition and cognitive flexibility in schizophrenia with and without comorbid substance use disorder. *Schizophrenia research*, 92, 168-180.



- Tomporowski, P.D., & Ganio, M.S. (2006). Short-term effects of aerobic exercise on executive processing, memory, and emotional reactivity. *International Journal of Sport and Exercise Psychology*, *4*, 57-72.
- Tsai, C.L., Pan, C.Y., Chen, F.C., Wang, C.H., & Chou, F.Y. (2016). Effects of acute aerobic exercise on a task-switching protocol and brain-derived neurotrophic factor concentrations in young adults with different levels of cardiorespiratory fitness. *Experimental Physiology*, *101*, 836-850.
- 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*, 973-979.
- Weiler, J., Hassall, C.D., Krigolson, O.E., & Heath, M. (2015). The unidirectional prosaccade switch-cost: electroencephalographic evidence of task-set inertia in oculomotor control. *Behavioural Brain Research*, *278*, 323-329.
- Weiler, J., & Heath, M. (2012a). The prior-antisaccade effect influences the planning and online control of prosaccades. *Experimental Brain Research*, *216*, 545-552.
- Weiler, J., & Heath, M. (2012b). Task-switching in oculomotor control: unidirectional switch-cost when alternating between pro-and antisaccades. *Neuroscience Letters*, *530*, 150-154.
- Weiler, J., & Heath, M. (2014a). Oculomotor task switching: alternating from a nonstandard to a standard response yields the unidirectional prosaccade switch-cost. *Journal of Neurophysiology*, *112*, 2176–2184.
- Weiler, J., & Heath, M. (2014b). Repetitive antisaccade execution does not increase the unidirectional prosaccade switch-cost. *Acta Psychologica*, *146*, 67-72.
- Weiler, J., Mitchell, T., & Heath, M. (2014). Response suppression delays the planning of subsequent stimulus-driven saccades. *PLoS One*, *9*, e86408.
- Winter, B., Breitenstein, C., Mooren, F.C., Voelker, K., Fobker, M., Lechtermann, A., ... & Knecht, S. (2007). High impact running improves learning. *Neurobiology of Learning and Memory*, *87*, 597-609.
- Wolohan, F.D., & Knox, P.C. (2014). Oculomotor inhibitory control in express saccade makers. *Experimental Brain Research*, *232*, 3949-3963.
- Wurtz, R.H., & Albano, J.E. (1980). Visual-motor function of the primate superior colliculus. *Annual Review of Neuroscience*, *3*, 189-226.
- Yanagisawa, H., Dan, I., Tsuzuki, D., Kato, M., Okamoto, M., Kyutoku, Y., & Soya, H. (2010). Acute moderate exercise elicits increased dorsolateral prefrontal activation and improves cognitive performance with Stroop test. *NeuroImage*, *50*, 1702-1710.

## Chapter 4

### General Conclusion

Chapter Two examined whether a 20-min single bout of aerobic exercise (via cycle ergometer) performed at moderate-to-heavy intensity (i.e., 80% of HR<sub>max</sub>) differentially influenced pre- and post-exercise pro- and antisaccade performance when ordered in an AABB paradigm (A=prosaccade, B=antisaccade). Consistent with previous work by my group, results from a pre-exercise assessment yielded a *unidirectional prosaccade switch-cost* – a result interpreted in line with the task-set inertia hypothesis’ contention that the executive demands of generating an antisaccade engenders a task-set that persists inertially and delays the planning of a subsequent prosaccade. Notably, however, at an immediate post-exercise assessment results did not reveal a reliable switch-cost. Accordingly, exercise provided an immediate ‘boost’ to cognitive flexibility and I believe that such a finding is attributed to enhanced neural efficiency within executive-mediated cortical networks.

Chapter Three examined for how long a single bout of exercise improves cognitive flexibility. In pursuing this objective, I had participants complete SD and MD saccades ordered in an AABB paradigm at a pre-exercise assessment and at assessments immediately, 30- and 60-min post-exercise. Results showed a reliable switch-cost at each assessment; however, the magnitude of the switch-cost was reliably reduced at the immediate and 30-min post-exercise assessment. Based on this finding I propose that a single bout of exercise improves cognitive flexibility for a period up to 47-min post-exercise.

I propose that Chapters Two and Three add importantly to the literature for at least two reasons. First, my results provide the first evidence demonstrating that a single bout of exercise *reliably* improves cognitive flexibility. As mentioned previously, earlier studies reported mixed findings regarding the benefit of exercise on task-switching and is a finding I attributed to methodological limitations in measuring cognitive flexibility. Accordingly, my results in combination with the extant literature examining inhibitory control and working memory provide convergent evidence that a single bout of exercise provides a benefit to each core component of executive function. Second, only limited research focused on the time course effects of a single bout of acute aerobic exercise on executive function and no previous work examined this issue for cognitive flexibility. Thus, my work provides the first evidence that a single bout of exercise provides more than a transient improvement to cognitive flexibility.

# Appendices

## Appendix A: Approval notice from the Office of Research Ethics, Western University for Chapter Two



**Date:** 30 October 2018

**To:** Dr. Matthew Heath

**Project ID:** 112323

**Study Title:** The effect of acute aerobic exercise on unidirectional switch-cost when alternating between pro- and antisaccades

**Application Type:** HSREB Amendment Form

**Review Type:** Delegated

**Meeting Date / Full Board Reporting Date:** 06/Nov/2018

**Date Approval Issued:** 30/Oct/2018

**REB Approval Expiry Date:** 28/Sep/2019

---

Dear Dr. Matthew Heath ,

The Western University Health Sciences Research Ethics Board (HSREB) has reviewed and approved the WREM application form for the amendment, as of the date noted above.

**Documents Approved:**

Document Name	Document Type	Document Date	Document Version
Diksha_LOI_Oct_23	Consent Form	23/Oct/2018	2

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions.

Sincerely,

Patricia Sargeant, Ethics Officer (ext. 85990) on behalf of Dr. Joseph Gilbert, HSREB Chair

*Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).*

## Appendix B: Approval notice from the Office of Research Ethics, Western University for Chapter Three



**Date:** 18 July 2019

**To:** Dr. Matthew Heath

**Project ID:** 114175

**Study Title:** Immediate and delayed executive benefits following a single-bout of aerobic exercise: an investigation using task-switching

**Application Type:** HSREB Initial Application

**Review Type:** Delegated

**Meeting Date / Full Board Reporting Date:** 06/Aug/2019

**Date Approval Issued:** 18/Jul/2019

**REB Approval Expiry Date:** 18/Jul/2020

---

Dear Dr. Matthew Heath

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above mentioned study as described in the WREM application form, as of the HSREB Initial Approval Date noted above. This research study is to be conducted by the investigator noted above. All other required institutional approvals must also be obtained prior to the conduct of the study.

**Documents Approved:**

Document Name	Document Type	Document Date	Document Version
Email Script	Email Script	05/Jul/2019	1
Eye Tracking Tool	Other Data Collection Instruments	17/Jun/2019	1
GLTEQ	Paper Survey	17/Jun/2019	1
LOI-1	Written Consent/Assent	05/Jul/2019	1
PAR-Q	Paper Survey	17/Jun/2019	1
Recruitment Advertisement	Recruitment Materials	05/Jul/2019	1

No deviations from, or changes to, the protocol or WREM application should be initiated without prior written approval of an appropriate amendment from Western HSREB, except when necessary to eliminate immediate hazard(s) to study participants or when the change(s) involves only administrative or logistical aspects of the trial.

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions.

Sincerely,

Patricia Sargeant, Ethics Officer (ext. 85990) on behalf of Dr. Joseph Gilbert, HSREB Chair

**Note:** This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).

# Curriculum Vitae

**Name:** Diksha Shukla

**Post-secondary Education and Degrees:** University of Waterloo  
Waterloo, Ontario, Canada  
2012-2017 B.Sc. Hons. Biomedical Sciences

The University of Western Ontario  
London, Ontario, Canada  
2018-2020 M.Sc. Kinesiology Candidate

**Honours and Awards:** Western Graduate Research Scholarship (WGRS)  
2018-2019

**Related Work Experience:** Teaching Assistant  
The University of Western Ontario  
2018-2019

## Publications:

Heath, M., **Shukla, D.** (2020). Aerobic exercise provides an immediate ‘boost’ to cognitive flexibility. *Frontiers in Human Neuroscience*. Manuscript submitted for publication.

**Shukla, D.**, Al-Shamil, Z., Heath, M. (2020). A single-bout of moderate intensity exercise improves cognitive flexibility: evidence from task-switching. *Brain and Cognition*. Manuscript submitted for publication.

**Shukla, D.**, Heath, M. (2020). A single-bout of exercise provides a persistent benefit to cognitive flexibility: evidence from oculomotor task-switching. *Brain and Cognition*. Manuscript submitted for publication.