Cognitive control, conflict monitoring, and aerobic exercise

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Kristopher Beyer

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Examining Committee membership

The following served on the Examining Committee for this thesis. The decision of the Examining Committee is by majority vote.

External Examiner	BERNADETTE MURPHY Professor, Faculty of Health Sciences, University of Ontario Institute of Technology
Supervisor	WILLIAM MCILROY Professor, Department of Kinesiology, University of Waterloo
Internal Member	W. RICHARD STAINES Professor, Department of Kinesiology, University of Waterloo
Internal Member	LAURA MIDDLETON Assistant Professor, Department of Kinesiology, University of Waterloo
Internal-external Member	DANIEL SMILEK Professor, Department of Psychology, University of Waterloo

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Abstract

Cognitive control includes a subset of top-down cognitive functions that allow flexible goal-directed behaviour that are often impaired in people with mental illness and in older adults. Even in healthy individuals, cognitive control ability is an important determinant of work and school success, physical health, and overall quality of life. Fortunately, modifiable lifestyle factors, including physical activity, may improve cognitive control in both healthy and impaired individuals. In particular, aerobic exercise benefits many types of cognitive function and may have its greatest impact on cognitive control – both after long-term training and even after a single session. The overall objective of this dissertation was to examine whether a single session of aerobic exercise impacts the ability of cognitive control to resolve conflict during choice reaction tasks. The dissertation examined the influence of a single session of aerobic exercise on behavioural performance and electroencephalography (EEG) markers of conflict measured during the flanker task – a choice reaction task that introduces conflict into information processing by including irrelevant distractor stimuli that may be congruent or incongruent with the target stimulus. A subset of this data was used to examine the relationship between behavioural and EEG markers of conflict during the flanker task. Behaviourally, aerobic exercise did not influence response accuracy or reaction time, but it reduced movement time. Aerobic exercise also did not influence the amplitude of the error-related negativity (ERN) or correct-related negativity (CRN) – EEG measures of brain activity related to monitoring conflict caused by error commission or flanker congruence. Across all exercise studies, aerobic exercise did not influence behavioural or EEG markers of conflict suggesting that previously observed exercise-induced performance improvements may be due to faster movement rather than enhanced cognitive control. Closer examination of the CRN as a measure of conflict-related brain activity,

however, indicated that it was not influenced by flanker congruence, nor was it associated with conflict-related changes in behaviour, demonstrating the need to further examine the role of the CRN in information processing. The accumulation of findings within this dissertation do not support a beneficial impact of aerobic exercise on the ability of cognitive control to resolve conflict during choice reaction tasks; however, this work also highlights the need to examine methodological shortcomings and differences between studies when assessing the influence of aerobic exercise on cognitive function.

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Chapter 1: Introduction

1.1 Overview

Cognitive control can be thought of as our ability to control our attention, behaviour, thoughts, and emotions to help us achieve our goals, especially in situations where those goals might conflict with our habits, instincts, or intuition[1–5] (a more explicit definition is provided in Section 1.2). Cognitive control helps us achieve our goals – big or small – in a wide variety of situations every day. Examples include not eating a tempting piece of chocolate cake that may conflict with our long term healthy-diet or weight-loss goals, navigating in a foreign country – as a driver or a pedestrian – in which they drive on the opposite side of the road to which we are accustomed, focusing on a conversation with a friend in the middle of a large group or a noisy restaurant, or completing an important project at school or work when we would rather be watching the latest season of our favourite show on Netflix.

Cognitive control is an important determinant of real-world behaviour across the lifespan and is often impaired in people with mental or behavioural disorders[2]. For example, in children, cognitive control is related to reading comprehension[6] and is directly associated with performance on English, mathematics, and science assessments[7,8]. In adolescents and young adults, cognitive control predicts avoidance of risky behaviour including smoking, alcohol and drug use, sex, and dangerous driving[9]. In young adults, cognitive control predicts reduced procrastination[10], better school- and work-related behaviour, such as hours worked and awards or promotions earned[11], and health protective behaviours, such as adherence to physical activity, diet, and medication plans[12,13]. In independent community-dwelling older adults, cognitive control predicts the ability to perform typical activities of daily living[14].

Conversely, cognitive control is often impaired in people with mental illness – such as anxiety[15], depression[16], attention deficit hyperactivity disorder (ADHD)[17], obsessive compulsive disorder (OCD)[18], post-traumatic stress disorder (PTSD)[19], autism[20], schizophrenia[21], and addiction to drugs, such as tobacco[22] and opiates[23], or behaviour, such as internet use[24] and gambling[25] – and may be affected following traumatic brain injury[26] or stroke[27]. Impaired cognitive control also contributes to age-related cognitive decline and is further affected with progression to mild cognitive impairment (MCI) and dementia[28–31]. Importantly, impaired cognitive control may be a harbinger of more serious problems: it occurs early in age-related cognitive decline but may be masked by compensatory recruitment of other cognitive processes and in otherwise healthy individuals it predicts future mental illness[28,31–37].

Because variability in 'healthy' cognitive control influences such a wide range of behaviour and predicts future mental illness and cognitive decline, it is clear that a better understanding of cognitive control – including how to optimize it in healthy individuals and how to identify and treat impairments before they progress to more insidious outcomes – could provide significant and broad societal benefits relating to education, productivity, health, safety, and, therefore, overall quality of life.

There are a number of interventions that have shown the potential to improve cognitive control in healthy individuals or rehabilitate it in those with impairments. Some pharmacological interventions are currently approved or are being evaluated for treatment of cognitive control impairments[38–40]. Various forms of transcranial stimulation have also been used to improve impaired cognitive control[41–44]. Behavioural training of cognitive control benefits the specific task trained, but transfer to other tasks is generally limited[44,45]. Coupling behavioural training with neurofeedback can also provide benefits to the trained task, but the transfer to other tasks is

unclear[44,46]. Modifiable lifestyle factors, such as cognitive engagement[47], social interaction[48,49], diet[50], meditation[51,52], and physical activity[53,54], are related to better cognitive control and thus show promise as interventions to improve it. These lifestyle factors are interesting because they do not involve training a specific task but generally benefit a wide range of cognitive function including cognitive control.

Physical activity is particularly interesting because it provides a wide range of beneficial effects on the brain and the rest of the body[53–57] and is, therefore, something most individuals should be engaged in for overall health and wellness[58,59]. Furthermore, a recent meta-analysis has shown that physical exercise and cognitive training interventions have similar effects on cognitive control[60]. Aerobic exercise, in particular, has positive effects on many types of cognitive function but seems to have its greatest effect on cognitive control[53,61,62]. Indeed, the selective effect of aerobic exercise on cognitive control has been observed following aerobic training programs and even transiently following a single session of aerobic exercise[61–65]. Understanding the mechanisms underlying these transient effects and the characteristics of the single session of exercise that elicits them may provide valuable guidance about how to optimize long-term exercise training programs to benefit cognitive control.

The overall objective of this dissertation was to examine whether a single session of aerobic exercise impacts the ability of cognitive control to resolve conflict during choice reaction tasks. The dissertation examined the influence of a single session of aerobic exercise on behavioural performance and electroencephalography (EEG) markers of conflict during the flanker task – a choice reaction task that introduces conflict into information processing by including irrelevant distractor stimuli. This dissertation is comprised of four specific studies. The specific objectives of each study are presented in Section 1.8.

1.2 Cognitive control

The terms cognitive control and executive function are used almost interchangeably by researchers to refer to a broad hypothetical construct describing very complex cognitive processing. The meaning and definition of both terms can vary slightly in different research contexts, but the various models of cognitive control and executive function contain common theoretical themes[1–5]. Within this dissertation, the term cognitive control is defined as a set of cognitive abilities – often aligned with one or more specific cognitive processes – that allow goal-directed behaviour, especially when conflicting behaviour is compelled by strong external stimuli or internal predispositions. Common across models of cognitive control are the following cognitive abilities: 1) creating and maintaining a representation of the current task or goal, 2) switching between different task or goal representations, and 3) inhibiting compelling sensory information, thoughts, emotions, or behaviours that are not relevant to the current task or goal[1–5]. Some cognitive control models associate specific cognitive processes with these core cognitive control abilities – working memory, cognitive flexibility, and inhibitory control, respectively – that, when combined, enable higher-order processes such as reasoning, problem solving, and planning[2,4]

Working memory combines the temporary storage of information – i.e., short-term memory – with the ability to manipulate this information[66,67]. It is useful as a cognitive control process because, at minimum, it enables the temporary storage and manipulation of current task and goal representations[2,4]. Interestingly, one of the most influential working memory models – the multicomponent model – includes its own conceptualization of cognitive control in the form of a central executive component in addition to multiple temporary storage components[66,67]. The

central executive, in the most recent iteration of this model, is primarily concerned with switching between task representations and controlling attention and, therefore, overlaps neatly with the function of the other two core cognitive control processes – cognitive flexibility and inhibitory control[2,4,66,67]. Working memory is often assessed using versions of the digit span task[68] or Corsi Block test[69] that require both short-term storage and manipulation of verbal or visuo-spatial information.

While task- or goal-relevant behaviour depends on the ability to maintain a representation of the task or goal, it is also useful to be able to quickly change the task or goal to ensure physical safety or take advantage of new opportunities as they arise. Cognitive flexibility – also called task switching or mental set shifting – describes this ability to move different task or goal representations in and out of working memory, that is, to 'switch' between these representations[2,4,70]. Cognitive flexibility is often assessed using sorting tasks, such as the Wisconsin Card Sorting Task[71], that require quickly changing the dimension (e.g., color, shape, number) that items are sorted on.

Finally, in order to enhance or bias behaviour that aligns more-closely with internally-held goals or intentions, inhibitory control allows the selective suppression of compelling but irrelevant or undesirable sensory information, thoughts, emotions, and behaviours[2,4]. As implied by this conception, inhibitory control can be applied at different levels of information processing[2]. At the perceptual level, inhibitory control enables suppression of attention to some stimuli in favour of others – often called selective or focused attention, attentional control, or executive attention. Cognitive inhibition enables suppression of compelling mental representations such as unwanted thoughts or memories. Inhibitory control can also be applied to suppress emotions that may arise from sensations, thoughts, or memories and promote

undesirable behaviour or it can be applied to directly suppress behaviour itself. Regardless of the level at which it is applied, inhibitory control often delays an inappropriate behaviour long enough to allow more complete processing of relevant information and selection of an appropriate response. Common assessments of inhibitory control include the Stroop[72], Simon[73,74], and flanker task[75] that require the inhibition of irrelevant information or prepotent stimuls-response pairings to successfully perform the task.

Another early but influential model of cognitive control describes these cognitive control abilities as emerging from the properties of the prefrontal cortex (PFC)[3]. In this model, tasks or goals are represented by patterns of activity maintained by the PFC that bias other networks throughout the CNS to promote appropriate task- or goal-relevant behaviour as it competes with other behaviour arising from irrelevant internal or external stimuli. The PFC, therefore, acts as the temporary and flexible storage for the representation of the current task or goal and influences behaviour through its broad connections to sensory, memory, emotional, and motor networks.

More recent neuroimaging research has extended this attribution to a distributed cognitive control network centering around the dorsolateral prefrontal cortex (dlPFC) with connections to other frontal regions, parietal and temporal regions, the anterior cingulate cortex (ACC), and specific subcortical areas[76,77]. This cognitive control network can also flexibly engage other networks, such as the dorsal attention network or the default mode network, to enlist focused external attention or autobiographical planning in support of goal-directed cognition[78]. As noted above, these broad connections allow the dlPFC to participate in the maintenance of task or goal representations and to exert influence on the sensory information, thoughts, emotions, and motor responses that shape behaviour. Additionally, the connection

between the dlPFC and ACC allows the regulation of cognitive control through the detection of events or conditions, such as reduced performance or information processing conflict, that signal a need for enhanced cognitive control.

1.3 Conflict and conflict monitoring

As mentioned, one of the core abilities of cognitive control is to resolve competition between incompatible behaviours by suppressing compelling sensory information, thoughts, emotions, or motor responses that are not relevant to the current task or goal[1–5]. Conflict, therefore, can be broadly defined as any behavioural competition of this type that must be resolved by cognitive control. More narrowly, conflict is easily observed in tasks such as the Stroop[72], Simon[73], and flanker task[75] that are often used to assess inhibitory control[2,74,79]. These tasks present stimuli that contain irrelevant features that map to a response that is incongruent with the desired or correct response. In this context, conflict may be defined as the competition between these incongruent stimulus-response pairings[80]. Conflict has been observed at the cortical level in the form of simultaneous activation of both contralateral and ipsilateral motor cortices on incongruent but not congruent trials despite exhibiting only an overt correct behavioural response[81]. At the muscle, a subset of correct responses contain EMG activity on the incorrect response side prior to activation of the correct response also indicating the simultaneous activation of conflicting response pathways[74]. Finally, the influence of conflict on behaviour can be observed in the form of slower responses or more errors on incongruent trials and is often quantified as the difference in behaviour between incongruent and congruent trials[74,79,82].

In the original conflict monitoring model[83] and the updated expected value of control theory[84] it is posited that a major function of the ACC is to monitor signals, such as conflict, that indicate the need for cognitive control and then specify additional control as appropriate. The previously mentioned connection between the ACC and dlPFC allows this specification[76,77]. The upregulation of cognitive control after high conflict trials can be observed behaviourally. For example, participants respond both faster and more accurately on incongruent trials if they follow an incongruent trial compared to a congruent trial[79,82,83,85]. EEG and fMRI studies support the putative role of the ACC in conflict monitoring by indicating that it responds to high levels of conflict[82,86–92]. Furthermore, this ACC activity related to conflict predicts frontoparietal network activity and the magnitude of behavioural adjustment on the following trial supporting the role of the ACC in specifying the need for cognitive control[82,90,93–95].

1.4 Flanker task

Choice reaction tasks, such as the Stroop[72], spatial Stroop[96], Simon[73,74], and flanker task[75], are commonly used to demonstrate and assess the ability of cognitive control – specifically, inhibitory control – to resolve conflict introduced by irrelevant distractor information and/or prepotent stimulus-response pairings. From these common tasks, the flanker task was chosen for use in this dissertation based on the following criteria: 1) it has previously been used to demonstrate an exercise-induced impact on cognitive control[64,65], 2) it has been used extensively to demonstrate the relationship between conflict monitoring and cognitive control processes[82,85,87,89,90], 3) it allows for a physical response from which reaction time and movement time can be obtained, and 4) the target stimulus is always in the same location reducing eye movement that would create EEG artifact.

During the flanker task, participants must make a directional choice response to a relevant central target stimulus while disregarding irrelevant stimuli that flank the target. These flanker stimuli create conflict particularly when they indicate a response that is incongruent with the target stimulus[74,79]. The flanker task requires cognitive control – which could be further categorized as inhibitory control at the level of perception (i.e., selective attention) – to restrict attention to the central target while ignoring the flanker stimuli[2].

Behavioural measures (e.g., reaction time, response accuracy) are often used to index the conflict created by flanker stimuli in the incongruent condition (i.e., flankers indicate a different response from target) relative to the congruent condition (i.e., flankers indicate the same response as the target) or a neutral condition (i.e., flankers do not indicate a response). During the flanker task, mean reaction time is longer and response accuracy is lower for incongruent than congruent or neutral trials[75,83,86,87,97]. These behavioural differences between congruent and incongruent trials are taken as evidence that the incongruent flankers cause conflict, which is often quantified by calculating the conflict effect (also called congruency effect or interference effect), the difference in mean reaction time or response accuracy between congruent and incongruent trials[79].

These behavioural indices of the interference or conflict caused by incongruent flanker stimuli are supported by electrophysiological evidence. The P3 is a stimulus-locked electroencephalography (EEG) event-related potential (ERP) component that is thought to represent attention and memory-related processing of a stimulus in order to update the representation of that stimulus within the context of the ongoing task[98,99]. Briefly, the amplitude of the P3 component is thought to reflect the amount of attentional resources devoted to the underlying memory-updating processes, while the latency indicates the time taken to evaluate the

stimulus[99]. While performing the flanker task, mean P3 amplitude is lower and mean P3 latency is longer in incongruent trials compared to congruent trials[64,65,100–102]. The decrease in amplitude may be interpreted as an indication of the higher cognitive demand of performing incongruent trials[99], attributable to the conflict created by the flanker stimuli. Similarly, the longer stimulus evaluation time in incongruent trials indicated by the increase in P3 latency may be attributed to the conflict created by the flanker stimuli.

High conflict not only influences performance on the current trial, it also influences performance on subsequent trials. On back-to-back high-conflict (i.e., incongruent) trials, different behavioural adjustments occur on the second trial depending on the success of the first trial: participants react faster if they were successful on the first high conflict trial[82] or slower if they were unsuccessful[94]. These behavioural adjustments have been attributed to a mechanism by which conflict monitoring processes signal a need for increased cognitive control in order to reduce or more quickly resolve the conflict on subsequent trials[83]. Indeed, experimental evidence using functional magnetic resonance imaging (fMRI) indicates that these behavioural adjustments are associated with ongoing cortical activity in the ACC and PFC related to conflict and performance monitoring and cognitive control, respectively[87,93]. That is, ACC activity reflects conflict and performance on the current trial and predicts PFC activity and behavioural adjustment (i.e., change in reaction time) on the subsequent trial. EEG data during the flanker task reveals a similar relationship between performance monitoring and subsequent behaviour. The error-related negativity (ERN) is a response-locked EEG ERP component that is thought to reflect ACC activity related to conflict monitoring during error commission[103,104]. When ICA is used to identify an independent component that accounts for the ERN, single-trial ERN

amplitude on error trials predicts the magnitude of the behavioural adjustment on the subsequent trial[90].

1.5 Aerobic exercise, conflict, and cognitive control

In addition to the well-known cardiovascular health benefits, aerobic training and fitness may also provide cognitive benefits throughout adulthood[53,54,105,106] although these benefits are often modest and inconsistent across studies[107]. Older adults who are already at risk for developing dementia (i.e., they have some form of mild cognitive impairment) show improvement in scores on tests designed to screen for dementia and performance on other tests of cognitive function including attention, memory, and cognitive control after participating in an aerobic exercise training program[108,109]. Furthermore, older women who reported being physically active at any point in their life had a lower risk of cognitive impairment later in life [110]. Healthy older adults may also benefit from regular physical activity. In older adults without MCI or dementia, physical activity and fitness are associated with better cognitive function including performance on tasks measuring memory and cognitive control[111–114]. As well, in healthy older adults, long-term aerobic exercise training improves performance on tasks that measure a wide range of cognitive function including response speed, memory, mental flexibility, cognitive control, attention, distractor interference, inhibition, and conflict[61,62,113,115,116] but appears to have the greatest influence on those tasks involving some form of cognitive control[61,62]. In a meta-analysis of 29 randomized control trials including 2049 adults of all ages (i.e., ≥ 18 years old), aerobic training lasting at least one month improved measures of attention and processing speed, cognitive control, and memory[117]. Age did not moderate the relationship between aerobic training and any of these cognitive functions

indicating that younger adults may benefit cognitively as much as older adults from aerobic training. However, compared to older adults, relatively few studies have examined how aerobic training and fitness influence cognition in young or middle-aged adults creating a gap in the literature[53,54,118]. Furthermore, while another meta-analysis of randomized controlled trials found that the many studies examining aerobic training programs in older adults improved aerobic fitness and at least one aspect of cognitive function, the benefits were usually modest, inconsistent across studies, and not necessarily linked to improvements in aerobic fitness[107]. Overall, while evidence is accumulating that aerobic training and fitness may provide cognitive benefits, the exact nature of these benefits, especially in young healthy adults, and their link to aerobic exercise remain unclear.

Experimental evidence also supports transient improvements in cognitive function after a single session of exercise, but the magnitude and nature of these benefits also remain unclear. Narrative reviews[63,119] and more recent meta-analyses[120,121] indicate that a single session of exercise has an overall small but significant positive influence on the performance of cognitive tasks. The most common behavioural measures of performance on cognitive tasks are speed or accuracy. Both types of measure may be influenced by exercise on a wide range of behavioural tasks designed to examine various cognitive processes. Improvement in speed occurs on a wide range of tasks designed to measure cognitive processes such as simple information transfer[122] (e.g., simple reaction time), more complicated information processing[123,124] (e.g., choice reaction time, go/no go), visual search[125], and various forms of cognitive control[122,123,126,127], attention[128], memory[129], and intelligence[130]. Performance on cognitive tasks that involve some form of decision making can also be assessed by a measure accuracy. Aerobic exercise has also been

shown to improve accuracy on a variety of tasks designed to measure cognitive processes such as visual search[125], memory[131,132], attention[133].

Most reviews and meta-analyses agree that a single session of aerobic exercise influences some types of cognitive tasks more than others, but they do not seem to agree on which tasks benefit the most. It has been variously suggested, however, that the effect on cognitive processes related to cognitive control – attention, cognitive control, inhibitory control, decision-making, working memory, and crystallized cognition – is greater compared to other tasks but the selective benefit to each of these cognitive processes is far from unanimous[63,119–121].

Findings indicating the influence of a single aerobic exercise session on behaviour (i.e., response speed and accuracy) during the flanker task are equivocal. Most studies agree that exercise does not influence response accuracy regardless of flanker congruency[64,65,100–102,134,135]; although, one recent study has shown that response accuracy increases significantly more following active aerobic exercise compared to a passive movement control condition[136]. This difference in response accuracy change was most prominent in incongruent trials but the authors did not interpret it as meaningful because it was primarily driven by a decrease (~2%) in accuracy after passive movement along with a slight, but not statistically significant, increase (<2%) in accuracy after active exercise. However, they did concede the possibility that aerobic exercise may act to ameliorate a decline in response accuracy, particularly on the incongruent trials, by maintaining attention that may otherwise wane over time.

The influence of a single session of aerobic exercise on response time is also unclear. Some of these studies indicate that response or reaction time can be improved by exercise. During exercise, response time decreases during the flanker task regardless of flanker congruence and exercise has no influence on stimulus- or response-level flanker interference[134].

After exercise, response time also decreases regardless of flanker congruence[101,102]; however, some studies have shown a greater effect on response time during incongruent trials indicated by a decrease in the flanker interference effect[64,65] or an interaction between exercise and flanker congruence[64]. However, where effects of aerobic exercise on response time do exist, it is unclear whether they can be attributed to changes in the speed of CNS processing or peripheral movement-related processes. When EMG is used to partition response time into reaction time and movement time during simple and choice reaction tasks, the existing evidence indicates that decreased response time during aerobic exercise can be attributed to decreased movement time rather than decreased reaction time[137–139]. Some evidence suggests that the observed decrease in flanker task response time during exercise could be explained by an improvement in motor processes similar to that seen in simple and choice reaction tasks but the examination of reaction time and movement time using EMG is required to confirm this explanation[134].

P3 amplitude consistently increases after exercise regardless of flanker congruency which has been interpreted as indicating an overall increase in available attentional resources allowing for more resources to be allocated to stimulus updating[64,65,100–102]. Contrarily, P3 latency can decrease after exercise regardless of flanker congruency[102] but there is a greater influence during incongruent flanker trials as indicated by an interaction between exercise and flanker congruence[100,101] indicating that, while P3 latency is normally shorter for congruent than incongruent trials, this difference may disappear following exercise.

Based on the relationship between attentional control and conflict monitoring[93], previous research has hypothesized that this increase in attentional control (i.e., increased P3 amplitude) may reduce conflict and subsequently reduce the amplitude of the ERN[135]. While this examination did not reveal an influence of exercise on the ERN[135] considerable methodological

limitations warrant further investigation. For example, they performed the flanker task after heart rate returned to within 10% of baseline which, they reported, as a mean time of 40.1 minutes with a standard deviation of 13.9 minutes. The variability of this timing could introduce variability into the data if the time course of the effect of exercise is not directly related to heart rate recovery. As well, a meta-analysis has shown that the greatest positive effects of exercise occur within 15 minutes of cessation[121].

1.6 Parameters of aerobic exercise and cognitive benefits

While narrative reviews[63,119] and more recent meta-analyses[120,121] indicate an overall small but significant positive influence of a single session of exercise on the performance of cognitive tasks, these reviews also point to a large number of experimental studies that find a single session of exercise has no influence or even a negative influence on performance of some cognitive tasks. This wide range of effects has helped to identify a number of exercise parameters that moderate the influence of exercise on cognition.

Exercise parameters such as mode, duration, and intensity can influence how aerobic exercise influences performance on concurrent or subsequent cognitive tasks. Previous research has employed a wide range of exercise parameters when exploring the relationship between exercise and cognitive function, so the effects of individual characteristics can be hard to discern from the literature. However, meta-analyses make it clear that certain exercise parameters are associated with greater positive effects on behavioural performance measures while performing cognitive tasks.

A wide range of exercise intensity can benefit cognitive task performance, but exercise intensity may influence the timing of the performance improvement. Narrative reviews and

recent meta-analyses agree that moderate intensity exercise has the most robust positive influence on a wide range of cognitive tasks both during and after exercise[63,119–121]. During exercise at higher intensity, performance on some cognitive tasks may suffer[63,120] but these negative effects don't usually last beyond the end of the exercise session. As well, even at extreme intensities, performance on many cognitive tasks can benefit after exercise has completed; although, this improvement may be delayed compared to after exercise at moderate intensity[63,120,121]. On the other hand, lower-intensity exercise has little influence on cognitive task performance during exercise but can have a positive influence on cognitive performance immediately after exercise[121]. While these reviews suggest that exercise intensity clearly moderates the relationship between exercise and cognitive task performance, it is important to note that this relationship is not always as clear in experimental studies[140] possibly related to an interaction between exercise intensity and other exercise characteristics such as duration, participant characteristics such as fitness, and task characteristics that can influence the relationship between exercise and performance improvements[63,119–121].

As with intensity, narrative reviews and recent meta-analyses agree that there is an optimal range of exercise duration[63,119–121]. Exercise sessions that last between 20 and 60 minutes produce robust improvements on performance of a wide range of cognitive tasks both during and after exercise[63,119–121]. Shorter exercise sessions often have no influence or even a negative influence on cognitive task performance during exercise with no change in performance lasting beyond the completion of exercise[120,121]. As may be expected then, even in longer exercise sessions there may be no change or even a negative change in cognitive task performance during the first 20 minutes of exercise before improvement begins to occur for the remainder of the session and beyond the completion of exercise[120,121]. Exercise lasting longer than 60 minutes

often has a negative influence on cognitive task performance both during and after exercise possibly due to fatigue, dehydration, and/or hypoglycemia[63,119,120].

Other exercise characteristics may also moderate the influence that exercise has on cognitive task performance. Mode is one characteristic that moderates this relationship[120]. Running has an overall negative influence on cognitive task performance during exercise with a small positive influence after exercise completion. In contrast, cycling has a small positive influence on cognitive task performance during exercise with a much larger influence after exercise completion. Regardless of the modality, optimal cognitive task performance, at least on reaction time tasks, occurs at the freely chosen work rate (e.g., walking speed or cycling pedal rate)[119].

In summary, moderate intensity (i.e., 40 to 59 % VO_2 reserve) and duration (i.e., 20 to 60 minutes) cycling exercise that allows the exerciser to freely choose a pedal rate produces the most robust benefits for cognitive task performance. This type of exercise is appropriate for healthy young and older adults and is recommended by to be performed 3-5 times per week totaling at least 150 minutes to achieve and maintain cardiorespiratory and other health benefits[58,59]. Therefore, to avoid confounders such as fatigue and dehydration, to maximize the positive influence of exercise, and to examine the influence of exercise already appropriate for and performed by a large portion of the population this dissertation focused on moderate intensity and duration aerobic exercise and its influence on cognitive task performance.

1.7 Potential neural mechanisms linking exercise and cognition

Over 40 years ago, it was first hypothesized that improved cognitive task performance following a bout of physical exercise may be mediated by arousal[141]. This hypothesis was

expanded upon by suggesting modulatory catecholamine neurotransmitters as mediators of this exercise-induced arousal[142]. It was postulated that these catecholamines, specifically epinephrine and norepinephrine, were diffusely secreted throughout the central nervous system by projections from the brain stem reticular formation to control cortical activation and behavioural arousal. The reticular formation was purported to be activated by afferent input during exercise, so the right dose of exercise could lead to an increase in arousal appropriate to improve cognitive task performance.

Behavioural arousal is controlled by a group of brainstem nuclei, sometimes called the, ascending arousal system, that modulate activity in the rest of the central nervous system. Individually, some of these nuclei also influence mood, attention, and memory making this system an intriguing candidate underlying the selective effects of aerobic exercise on these cognitive processes. These brainstem nuclei consist of neuronal cell bodies that project axons to various regions of the brain where they secrete modulatory neurotransmitters into the target tissue when activated. Neurotransmitters used by these systems include acetylcholine (ACh) and the monoamines epinephrine (E), norepinephrine (NE), serotonin (5-hydroxytraptamine, 5-HT), dopamine (DA), and histamine (H). In the target tissue, these neurotransmitters usually bind with metabotropic receptors to influence synaptic transmission. The specific influence at any given synapse depends upon the receptors present and the extracellular concentration of neurotransmitter. Each nucleus-neurotransmitter system has a discrete region of influence, but many have widespread projections to nearly the entire brain. As such, these brainstem nuclei form a collection of several discrete but interconnected and often overlapping systems that modulate activity throughout the CNS.

Indeed, accumulating evidence does suggest that aerobic exercise influences the activity of the nuclei that form the ascending arousal system. In rodents, concentrations of various modulatory neurotransmitters (i.e., dopamine, norepinephrine, and serotonin) increase in specific brain regions during and after aerobic exercise. A single session of aerobic exercise influences norepinephrine concentration or metabolism in the parietal[143] and frontal cortex[144,145], the preoptic area and anterior hypothalamus[146,147], and the striatum[148] but not the hippocampus[149]. Aerobic exercise influences dopamine concentration or metabolism in the striatum[148,150,151], preoptic area and anterior hypothalamus[146,147,152], and hippocampus[149]. Finally, aerobic exercise influences serotonin concentration or metabolism in the parietal[143] and frontal cortex[153] and the hippocampus[153–155] but not the preoptic and anterior hypothalamus[146,147,152].

1.8 Research objectives

As previously noted, the overall objective of this dissertation was to examine whether a single session of aerobic exercise impacts the ability of cognitive control to resolve conflict during choice reaction tasks. This dissertation is comprised of four specific studies with the following objectives.

Study 1: The primary objective was to examine how CNS and non-CNS motor processes contribute to changes in flanker task performance previously observed during and after a single aerobic exercise session. To accomplish this objective, electromyography was used to partition behavioural response times into reaction time, a measure of CNS processing speed, and movement time, a measure of non-CNS motor speed.

To test the assertion that aerobic exercise improves performance during certain behavioural tasks by reducing conflict, the next two studies focused on examining how a single session of aerobic exercise influences conflict-related brain activity.

Study 2: The error-related negativity (ERN) was examined using conventional electroencephalography (EEG) event-relate-potential (ERP) techniques. The ERN is a purported measure of conflict-related brain activity during incongruent flanker trials with high enough conflict to cause an incorrect response. While this is the traditional EEG method used to examine conflict-related brain activity, more recent research has indicated that conflict and error commission may have separable effects on conflict-related brain activity. Therefore, interpretation of the ERN may be confounded by the inclusion of both conflict- and error-related brain activity. This limitation informed the objectives of the subsequent studies.

Study 3: The primary objective was isolate conflict-related brain activity from error-related brain activity and examine how this brain activity is influenced by a single session of aerobic exercise. To accomplish this, novel EEG processing techniques including independent component analysis (ICA) were used to reveal the correct-related negativity (CRN), a measure of response-related brain activity that is not visible using conventional EEG ERP techniques and is purported to be sensitive to conflict.

Study 4: Based on the findings of the previous two studies, we recognized the need for a better understanding of the relationship between brain activity and behavioural performance linked to conflict. Therefore, in the fourth study, we examined the relationship between brain activity and

behavioural performance caused by conflict at the single-trial level. We also tested predictions about the influence of conflict on subsequent trial conflict and performance based on the dynamic relationship between conflict monitoring and conflict control networks and their influence on optimization of information processing. Novel EEG techniques were again required to ascertain a single-trial CRN to measure brain activity related to conflict. Supplementary analyses were employed to confirm that our single-trial CRN reflected brain activity related to conflict but separable from error commission. The identification of a single-trial measure of brain activity related to conflict and examination of its relationship with behaviour and cognitive control in this study represents the first step towards directly exploring the influence of aerobic exercise on the dynamically changing relationships between cognitive control, conflict, and behavioural performance.

Chapter 2: Study 1

A single aerobic exercise session accelerates movement execution but not central processing

Adapted from: Beyer KB, Sage MD, Staines WR, Middleton LE, McIlroy WE. A single aerobic exercise session accelerates movement execution but not central processing. *Neuroscience.* 2017;346:149-159.

2.1 Introduction

Central nervous system (CNS) speed of processing is an important, broad indicator of cognitive function that may be improved with aerobic exercise. Speed of processing has been defined as the "maximum rate at which elementary cognitive operations are executed[156]" and its utility as an indicator of overall cognitive function was first argued due to its predictable changes across the lifespan and its association with other higher-order cognitive function[156]. Indeed, speed of processing improves from childhood to young adulthood[157] but declines into older age[158,159] or in various states of CNS disease or injury[160–165]. Importantly, this decline in speed of processing may contribute to, or at least indicate, decline in higher-order cognitive function[156,159,166]. Conversely, physical activity is associated with important beneficial changes in brain structure and cognitive function, including speed of processing[53]. Most notably, speed of processing is purported to improve robustly following long-term participation in aerobic activity[61,111] and transiently following a single session of aerobic exercise, even in young healthy

adults[63,120,121]. However, this evidence remains controversial due, in part, to the use of different measurement approaches.

To estimate CNS speed of processing, response time is often measured from the onset of a stimulus (e.g., a light) to the completion of a behavioural response (e.g., pressing a button). As such, response time captures both premotor and motor components of the behavioural response but can be partitioned into reaction time and movement time representing these premotor and motor components, respectively. Traditionally, a mechanical measure of the onset of a behavioural response (e.g., lifting a finger from a button before completing the response by pressing another button) has been used to partition response time into reaction time and movement time. However, when measured as such, reaction time captures both premotor components and the initial motor components of movement execution such as muscle excitation-contraction, force generation, and some initial movement, so we would still consider this a measure of response time. To overcome these confounds, electromyography (EMG) has been used to partition response time into reaction time and movement time[167]. Using this method, reaction time is measured from stimulus onset to EMG onset capturing premotor components of the response without being confounded by initial motor components and, therefore, providing a better estimate of CNS speed of processing.

Inconsistency in the use of these measures to estimate CNS speed of processing may account for differences in how speed of processing is influenced by a single session of aerobic exercise. An exercise-induced improvement in speed of processing in a wide variety of cognitive tasks has been inferred from observed decreases in response time[63,120]. Conversely, a handful of studies have examined exercise-induced changes in speed of processing in young healthy adults by partitioning response time into reaction time and movement time using EMG[137–139].

Davranche et al. (2005) had adults perform a choice reaction task during 20 minutes of moderate-intensity (50% maximal aerobic power) cycling exercise and at rest. Response time was shorter after exercise compared to at rest owing to shorter movement time with very little change in reaction time. A follow-up study, showed the same results for a simple reaction task[139]. Audiffren et al. (2008) had young adults perform blocks of a choice reaction task every 6 to 8 minutes during and after a moderate-intensity 35-minute cycling session and during a rest session. During exercise, response time gradually shortened, reaching a minimum between 15 and 20 minutes, and returned to baseline immediately after exercise. Based on analysis of selected time points during exercise and rest, shortened movement time but not reaction time was responsible for the shorter response time. These studies indicate that exercise-induced shortening of response time may have more to do with faster movement execution than faster CNS processing, at least for relatively simple behavioural tasks. The influence of a single session of aerobic exercise on speed of processing during more complex tasks is less clear.

Unlike simple and choice reaction tasks, there is evidence to suggest that speed of processing during the flanker task[75], or incongruent flanker trials in particular, may be selectively influenced by aerobic exercise. When performing the flanker task, one must choose a response based on relevant information provided by a central target stimulus while disregarding potentially conflicting irrelevant information from flanking stimuli that may be congruent or incongruent with the response to the target. Both during and after aerobic exercise, response time decreases during the flanker task have been observed regardless of flanker congruence and without any change in response accuracy[101,102,134]. Davaranche et al. (2009) had adults perform a flanker task during two 15-minute moderate-intensity (mean 76% HR_{max}) cycling sessions and at rest. Response time was shorter during exercise than at rest, regardless of flanker congruency.

Kamijo et al. (2009) had both younger and older adult males perform a flanker task at baseline and immediately after 20 minutes of light- (mean 55% HR_{peak}) and moderate-intensity (mean 75% HR_{peak}) cycling exercise. For both younger and older adults, response time was shorter after moderate-intensity exercise than after light-intensity exercise or at baseline, regardless of flanker congruency. However, after exercise, some studies have shown a greater decrease in response time during incongruent than congruent trials[64,65]. Chang et al. (2015) had two groups of young adults perform the attention network test (which includes aspects of the flanker task) immediately after either 30 minutes of moderate-intensity (70-85% HR_{max}) cycling exercise or reading an exercise-related book. The congruency effect, the difference in response time typically found between incongruent and congruent flanker trials, was smaller in the exercise group than the reading group. Similarly, O'Leary et al. (2011) found that the congruency effect was smaller after young adults performed 20 minutes of moderate-intensity (60% HR_{max}) treadmill exercise compared to after seated rest or video-gaming. Since it is unlikely that there is a difference in movement time between congruent and incongruent trials, it is possible that the difference in response time can be accounted for by an additional decrease in reaction time during incongruent trials following exercise. Furthermore, a previous review has suggested that performance on tasks that involve blocking irrelevant stimuli, like incongruent flanker trials, is preferentially influenced by a single session of aerobic exercise[63] and the flanker task has been shown to involve frontal brain regions involved in selective attention [113] that are selectively influenced by fitness and long-term aerobic training[112,113,168]. Despite this evidence, it remains unclear whether exercise-induced decreases in response time during the flanker task can be attributed, at least partially, to decreased reaction time or to movement time only like in simple and choice reaction tasks.

Therefore, the primary purpose of this study was to separately examine the influence of a single session of aerobic exercise on speed of processing (reaction time) and movement execution (movement time) in young healthy adults during a flanker task. We hypothesized that aerobic exercise would influence reaction time and movement time differently. Specifically, we predicted that during and after aerobic exercise movement time during the flanker task would decrease similarly to that seen in previous studies regardless of flanker congruence but reaction time would only decrease during incongruent flanker trials accounting for the selectively greater influence of exercise on response times during incongruent flanker trials. Additionally, to replicate previous findings, we predicted that movement time during a simple reaction task would decrease during and after aerobic exercise but reaction time would not change. Revealing how a single session of aerobic exercise influences reaction time and movement time during simple and complex tasks is an important step in understanding how aerobic exercise influences the CNS.

2.2 Experimental procedures

Participants

Twelve healthy, young adults (6 female) volunteered to participate in this study. This study was approved by the Office of Research Ethics at the University of Waterloo and all participants provided written informed consent before participating. Participants were screened for exclusion criteria including musculoskeletal or neurologic disorders that may have affected their ability to perform the study and their readiness to exercise without requiring permission from their physician (Physical Activity Readiness Questionnaire, Canadian Society for Exercise Physiology, Ottawa, ON). One participant did not complete the study due to an irreparable

equipment malfunction. One participant was excluded from analysis due to an equipment malfunction that caused missing data. Therefore, 10 participants (5 female) were included in the final analysis.

Experimental protocol

Each participant visited the laboratory for three separate sessions: 1) screening and graded exercise test, 2) exercise session, and 3) non-exercise control session. All three sessions were performed at the same time of day for each participant. The first session preceded the second session by 2 to 13 days; the second and third session were either 2 or 3 days apart. The first session lasted 30 to 45 minutes while the last two sessions lasted approximately two hours each. The order of delivery of the last two sessions was counter-balanced.

Upon arrival for the first session, participants were provided information about the study before consenting to participate. During this initial session, participants received instruction and familiarization with the Rating of Perceived Exertion (RPE), the cognitive tasks that would be performed, and the magnetic-resistance recumbent cycle ergometer (Wynne 2.3R, Wynne Biomedical Ltd., New Dundee, ON). Participants then performed the graded exercise test to establish aerobic fitness levels and determine the work rate for the exercise session.

During the exercise session (Figure 2.1A), participants sat on a recumbent cycle ergometer for the entire session. Before exercising, participants sat quietly for two minutes while resting heart rate was measured and then performed one block of each cognitive task. Participants were then allowed five minutes to warm up before exercising for 40 minutes. During exercise, participants performed one block of each cognitive task every ten minutes (i.e., task blocks started at minute 0, 10, 20, and 30 of exercise). After completing the exercise, participants

sat quietly for 40 minutes and again performed one block of each cognitive task every ten minutes (i.e., task blocks started at minute 0, 10, 20, and 30 after exercise). The order of delivery of two cognitive tasks (i.e., simple reaction task and modified Eriksen flanker task) was constant for each participant but was counter-balanced across participants.

During the non-exercise control session subjects sat quietly on the recumbent cycle ergometer without pedaling. All other task conditions were the same between exercise and non-exercise control sessions.

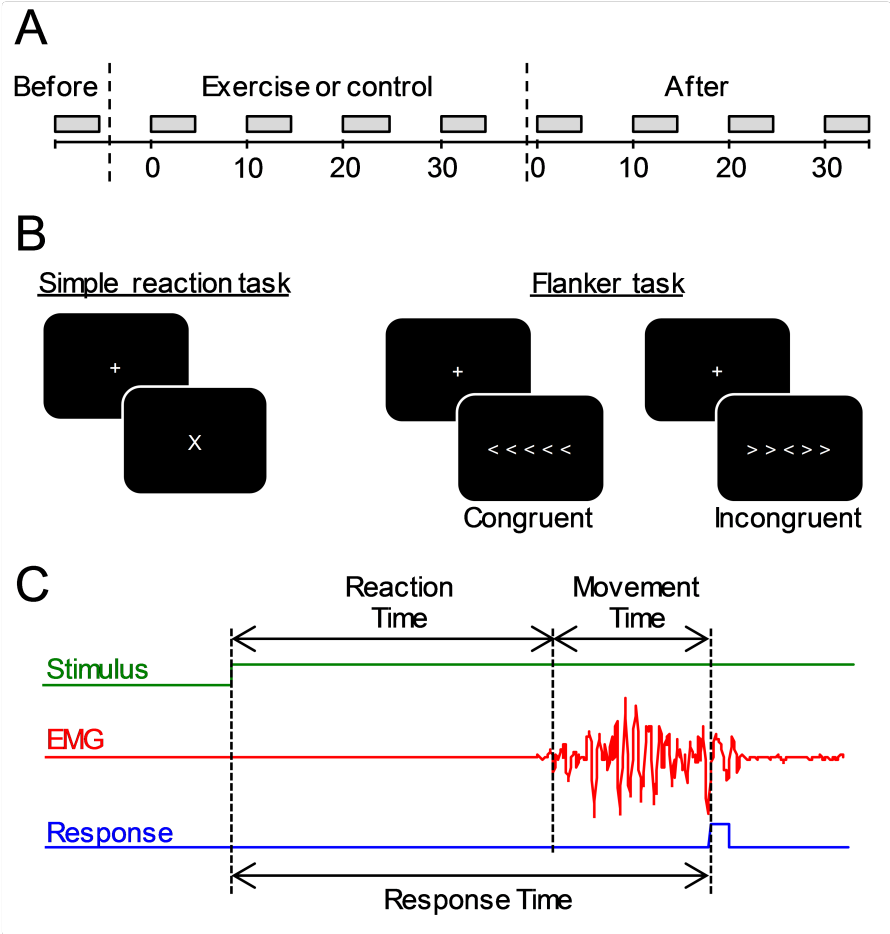

Figure 2.1. Study design and methods. (A) During the exercise and non-exercise control sessions, participants performed a block of cognitive tasks every 10 minutes before, during, and after exercising at a moderate intensity or sitting quietly on the cycle ergometer. (B) Each block of cognitive tasks consisted of a block of 30 simple reaction trials and a block of 60 modified Eriksen flanker trials, 30 congruent and 30 incongruent. In both tasks, participants responded to stimuli by raising their right or left arm laterally to shoulder height. (C) Reaction time was measured from stimulus onset to middle deltoid EMG onset. Movement time was measured from EMG onset to response completion, which occurred when the arm passed through a beam of light monitored by a photoelectric sensor.

Graded exercise test

Each participant performed a graded exercise test (GXT) on the cycle ergometer to measure peak oxygen consumption (VO_{2peak}) and determine the work rate for the exercise session. Before starting the test, participants were instructed to choose a comfortable rate while pedaling at work level 3 and then rested quietly for 2 minutes. The test started with the participant pedaling at the previously chosen comfortable rate at work level 1. Every minute the work level was increased by 1 until the participant chose to stop or could no longer maintain the chosen comfortable rate.

Throughout the test, respiratory gases were analyzed breath-by-breath (Vmax 229, SensorMedics Inc., Palms Springs, CA) and electrocardiogram (ECG) was measured continuously. Gas analysis and ECG were transmitted to computer software (Vmax Vision, SensorMedics Inc., Palms Springs, CA) for calculation of variables of interest [e.g., oxygen consumption (VO_2), respiratory exchange ratio (RER), and heart rate (HR)]. These variables were displayed in real-time and stored for offline processing and analysis. RPE was measured at the beginning of each work level. Offline, VO_2, RER, and HR were averaged over 20-second intervals. Resting VO_2 was the mean VO_2 during the 2-minute rest period prior to exercise. VO_{2peak}, RER_{peak}, RPE_{peak}, and HR_{peak} were calculated as the respective peaks achieved during the GXT. Oxygen uptake reserve (VO_2R) was calculated as the difference between VO_{2peak} and resting VO_2.

GXT results were compared to commonly used pre-determined criteria[169] to test whether each participant achieved a true VO_{2peak}. The primary criterion was an increase in VO_2 of less than or equal to 2.1 ml/kg/min after an increase in workload. Secondary criteria were a RER_{peak} greater than 1.1, RPE_{peak} greater than 9, HR_{peak} greater than 90 % of age-predicted (i.e., 220 –

age). To be deemed a true VO_{2peak} the primary criterion or at least two of the secondary criteria must have been achieved during the test; all subjects met these criteria.

Exercise and associated measures

During the exercise session, each participant performed a 40-minute session of exercise on a magnetic-resistance recumbent cycle ergometer. Exercise intensity was set and monitored using the work level, RPE, and HR coinciding with 40-59 % VO_2R during the participant's GXT. Throughout the warm-up and exercise participants were allowed to pedal at a self-selected comfortable rate while the work level was adjusted by the researcher to maintain the desired intensity. Each participant began the 5-minute warm-up pedaling at work level 1 while the researcher gradually increased the work level to that coinciding with 40 % VO_2R. During the 40-minute exercise session participants continued to pedal at a self-selected comfortable rate while the researcher adjusted the work level to maintain a HR in the range coinciding with 40-59 % VO_2R.

Pedal rate. A switch on the cycle ergometer indicated each revolution of the pedals and was used to calculate revolutions per minute (RPM).

Heart rate. For the GXT, exercise, and non-exercise control sessions ECG was collected continuously (EK-10, Burdick Inc., Milton, WI). Electrode sites at the center of the manubrium and bilaterally over the 5^{th} intercostal space along the mid-clavicular line were cleaned with abrasive gel and alcohol before electrodes (Positrace, ConMed, Utica, NY) were placed. Data were sampled at 1,000 Hz and stored for offline processing. ECG was used to calculate HR in beats per minute (BPM). During exercise, a real-time HR was calculated and displayed to the experimenter to monitor exercise intensity.

Rating of perceived exertion. RPE, using the CR10 scale[170], was used to monitor exercise intensity. Throughout the graded exercise test and exercise session, the participant was asked to verbally rate their perceived exertion on a scale from 0 (nothing at all) to 10 (very, very strong). During the exercise and control sessions, for the four blocks of cognitive tasks during exercise, participants were asked for their RPE before the first cognitive task, between the two cognitive tasks in the block, and after the second cognitive task.

Reaction time tasks and associated measures

Participants performed two reaction time tasks: simple reaction task and modified flanker task[75,87] (Figure 2.1B). Both tasks were delivered via custom software (LabVIEW, National Instruments, Austin, TX) projected onto a screen directly in front of the recumbent cycle ergometer so that stimuli were presented at eye level approximately 200 cm from the participant. Participants fixated on a point in the center of the screen while white stimuli were presented on a black background. The fixation point and all stimuli were approximately 23 cm high. Participants began each trial with their hands resting on two handles located lateral to the seat and responded to stimuli by raising their right or left arm laterally (i.e., shoulder abduction) to shoulder height.

Simple reaction task. In each trial a single stimulus, an X, was presented and participants were asked to respond by raising their right arm to the side (i.e., shoulder abduction) as quickly as possible. A stimulus was presented for 500 ms every 2 seconds and participants were allowed 1000 ms to respond. Each block consisted of 30 trials plus 6 randomly inserted 'catch' trials, in which no stimulus was presented, to prevent anticipation.

Modified Eriksen flanker. Participants performed a version of the Eriksen flanker task[75] modified to use arrows as stimuli instead of letters[87]. In each trial, a target stimulus was presented consisting of a right or left pointing arrow (i.e., > or <). The target stimulus was flanked by 4 additional arrows, two on each side, that were either congruent (< < < < < or > > > > >) or incongruent (< < > < < or > > < > >) with the target arrow. Participants responded by raising their right or left arm to the side (i.e., shoulder abduction) as quickly as possible as indicated by the target arrow. A stimulus was presented for 500 ms every 2 seconds and participants were allowed 1000 ms to respond. Participants did not receive any feedback during or after the flanker task indicating whether they responded in time or made an error. In each block 15 stimuli of each condition were presented in random order for a total of 60 trials.

Muscle activity. Bilateral middle deltoid EMG, time-locked to stimulus onset, was measured to determine the onset of muscle activity during responses. Electrode sites on the muscle belly of bilateral middle deltoids and on the left clavicle were cleaned with abrasive gel and alcohol. Electrodes (Kendall 130, Covidien, Dublin, IR) were placed 2 cm apart over each middle deltoid muscle belly. Another electrode was placed on the left clavicle to act as a ground. Data were amplified (x 500), filtered (10-1,000 Hz; AMT-8, Bortec Biomedical, Calgary, AB), sampled at 1,000 Hz, and stored for offline processing.

Response completion. Photoelectric sensors (Enhanced 50 Series, Eaton, Burlington, ON) were used to determine the point in time at which the participant's arm crossed the beam of light signalling completion of the response. Each sensor emitted and detected a reflected polarized beam of light. Sensors were placed on either side of the cycle ergometer so that the beam ran parallel to the midline of the cycle ergometer 40 cm away from (i.e., 34.6 cm lateral and 20 cm

above) the center of a handle located lateral to the seat. The voltage output indicating whether the beam was broken or not was sampled at 1,000 Hz and stored for offline processing.

Data processing

EMG signals were bandpass filtered (20-500 Hz), baseline corrected, and full-wave rectified before being low-pass filtered (50 Hz). EMG onset was determined using the following criteria: 1) full-wave rectified EMG exceeded a threshold equal to the mean plus 3 standard deviations of a 50-ms pre-stimulus baseline and 2) low-pass filtered EMG remained above this threshold for at least 25 ms.

Trials in both cognitive tasks were rejected if EMG onset or response completion was not properly detected (9 % of trials). In the flanker task, response and EMG error trials (1 and 10 % of trials, respectively) were also rejected. A response error occurred when the participant made a complete incorrect response as indicated by the photoelectric sensor indicating a break in the beam of light on the incorrect side. An EMG error occurred when a distinct pattern of EMG activity on the incorrect side preceded movement on the correct side indicating some movement with the incorrect arm but not enough to break the beam of light.

In all accepted trials (i.e., not rejected due to missing data or error) reaction time and movement time were calculated (Figure 2.1C). Reaction time was the time elapsed between stimulus onset and middle deltoid muscle activity onset. Movement time was the time elapsed between muscle activity onset and response completion.

Reaction times greater than 600 ms (representing approximately 1 % of the data) were deemed unlikely to represent true reaction time and were removed. Reaction time and movement time residuals were normally distributed as indicated by examination of skewness and kurtosis.

Statistical analysis

Planned comparisons examined our main hypotheses comparing movement time and reaction time for each task between the exercise and non-exercise control sessions during and immediately after exercise. Movement time, reaction time, and response accuracy at other time points as well as exercise characteristics were examined for descriptive purposes.

To examine reaction time and movement time, separate repeated-measures analyses of variance (ANOVA) were conducted with three factors: TASK (3 levels: simple reaction task, congruent flanker trials, and incongruent flanker trials), EXERCISE (2 levels: exercise and control), and TIME (9 levels: before exercise or control; minute 0, 10, 20, and 30 during exercise or control; and minute 0, 10, 20, and 30 of recovery after exercise or control). Planned comparisons were conducted using paired one-tailed t-tests computed from the model elements in the repeated-measures ANOVA to compare the exercise session to the non-exercise control session at minute 30 of exercise or control and minute 0 of recovery for each task. To examine response accuracy, a repeated-measures ANOVA was conducted with the same three factors as above, but TASK had only two levels (congruent and incongruent flanker trials). Paired t-tests were used to compare HR, RPE, and RPM while performing cognitive tasks during exercise to exercise alone in the exercise session and while performing cognitive tasks to sitting quietly in the control session. The degrees of freedom for all repeated-measures ANOVAs were adjusted using Huyhn-Feldt epsilon to account for violations of sphericity. Post hoc analyses of significant interactions and main effects in omnibus ANOVAs were performed using ANOVA or t-test. A significance level (α) of .05 was set for all statistical tests.

2.3 Results

Participant demographic, fitness, and exercise characteristics

Ten young healthy adults [5 female; mean (sd) age 24.4 (3.7) years] completed the study and were included in the final analyses. Individual and group mean demographic and GXT data are shown in Table 2.1 (males and females are separated for display only, no gender effect was analyzed).

Table 2.1. Individual participant demographic and graded exercise test data.

	Demographic				Graded Exercise Test		
ID	Sex	Age (years)	Height (cm)	Mass (kg)	HR_{peak} (BPM)	VO_{2peak} (ml/kg/min)	VO_2 norm group
Males							
1	M	23	175	89.5	197	41.5	Fair
3	M	28	180	93.5	204	42.6	Average
4	M	25	180	106.5	171	32.4	Poor
5	M	18	181	93.0	168	41.1	Fair
8	M	21	175	68.0	181	43.0	Fair
Females							
2	F	27	173	65.5	174	41.9	Good
6	F	23	173	56.0	195	52.3	Excellent
7	F	24	168	55.5	178	50.0	Very Good
10	F	31	165	48.5	189	32.6	Fair
11	F	24	173	68.5	177	44.7	Good
Mean		24.4	174.3	74.45	183.4	42.21	
SD		3.7	5.2	19.69	12.2	6.32	

HR = heart rate, VO_2 = volume of oxygen consumed. VO_2 norm groups are from Shvartz & Reibold 1990.

During the graded exercise test, all participants met the preset criteria for VO_{2peak}. Fitness was assessed by comparing VO_{2peak} to published normative data based on age and gender[171]. The

group mean (sd) VO_{2peak} was 42.21 (6.32) ml/kg/min, which would be in the fair to good normative groups depending on age and gender. Compared to the normative data, the female participants in this study were fitter than the male participants: all five male participants ranked average or lower while four of the five female participants ranked above average. During the exercise session, participants exercised at a mean HR of 73.5 % of HR_{peak} and a mean RPE of 4.49, which were both within the mean target ranges coinciding with 40-59 % VO_2R (Table 2.2). HR, RPE, and pedal rate were higher when performing the cognitive tasks during exercise compared to exercise alone (all $p < .005$).

Table 2.2. Exercise characteristics.

		Rest	Exercise
Target heart rate (% HR_{peak})	*min*		69.5 (4.3)
	max		79.1 (3.6)
Heart rate (% HR_{peak})	*exercise or rest only*	41.6 (5.3)	70.5 (6.0)
	with cognitive task	42.4 (5.0)	76.5 (6.9) *
	collapsed	42.0 (4.9)	73.5 (6.2)
Target RPE	*min*		3.40 (1.07)
	max		5.65 (1.20)
RPE	*exercise or rest only*	0.05 (0.12)	4.04 (1.14)
	with cognitive task	0.20 (0.21) +	4.94 (1.66) *
	collapsed	0.13 (0.15)	4.49 (1.37)
Pedal rate (RPM)	*exercise or rest only*		52.9 (3.7)
	with cognitive task		55.9 (5.0) *
	collapsed		54.2 (4.2)

Mean (SD). HR = heart rate, RPE = rate of perceived exertion, RPM = rotations per minute. * significantly higher than exercise alone ($p < .005$). + significantly higher than rest alone ($p = .01$).

Movement time

Figure 2.2 shows mean movement time at all time points for all tasks in both sessions. TASK and EXERCISE interacted to influence movement time ($F_{(2, 18)} = 7.77$, $p = .004$). Post hoc analysis revealed that mean movement time was shorter in the exercise session than the control session for all tasks with mean differences of 9.3 ms for the simple reaction task, 4.9 ms for congruent flanker trials, and 6.6 ms for incongruent flanker trials ($t_{(89)} = 6.17$ to 11.71, all $p <$ .001).

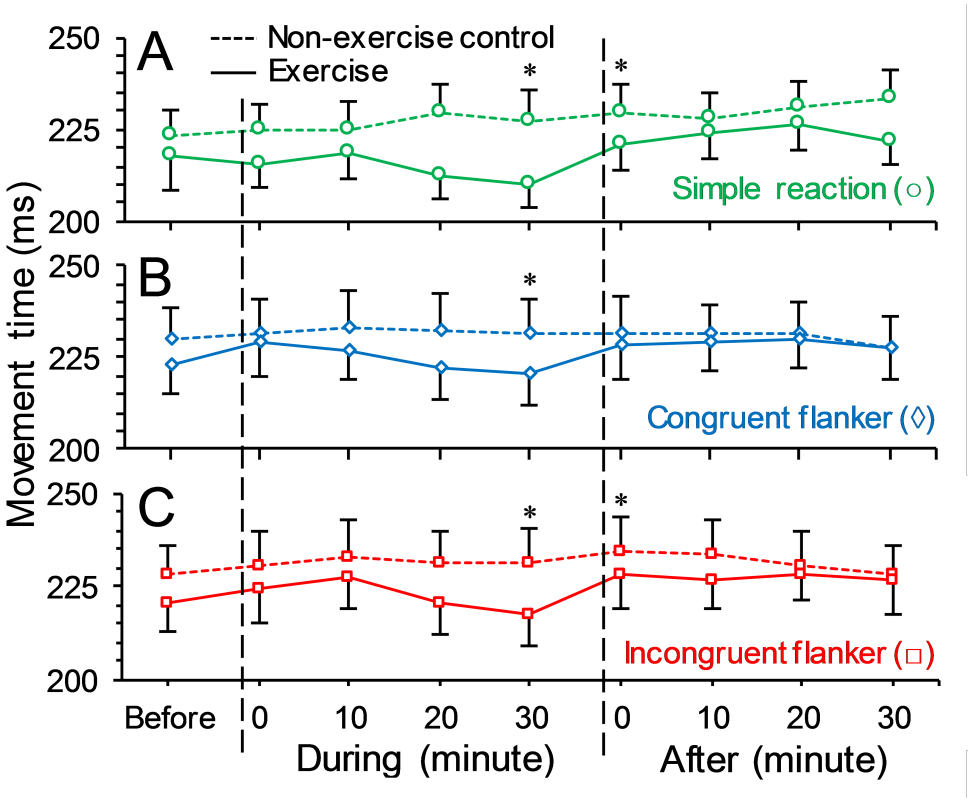

Figure 2.2. Movement time (mean ± SEM) at each time point before, during, and after exercise or non-exercise control for simple reaction task (A), congruent flanker trials (B), and incongruent flanker trials (C). Exercise or non-exercise control is denoted by vertical dashed lines. At minute 30 during exercise and minute 0 after exercise, movement time was shorter than non-exercise control for all tasks except for congruent flanker trials, which was only shorter than control during exercise (* $p < .007$).

Planned comparisons revealed that movement time at minute 30 of exercise was shorter than at minute 30 of non-exercise control for all tasks with mean differences of 17.2 ms for the simple reaction task, 10.6 ms for congruent flanker trials, and 13.7 ms for incongruent flanker trials (one-tailed paired $t_{(9)} = 4.48$ to 7.22, all $p < .001$). Movement time remained shorter than control at minute 0 after exercise for all tasks but was only statistically different for the simple reaction task (7.2 ms, one-tailed paired $t_{(9)} = 3.44$, $p < .001$) and incongruent flanker trials (6.0 ms, one-tailed paired $t_{(9)} = 2.49$, $p = .007$), not congruent flanker trials (3.7 ms, one-tailed paired $t_{(9)} = 1.54$, $p = .063$).

In addition, movement time appeared to change systematically over time across all three tasks in the exercise but not the control session. These results should be interpreted with caution since the interaction between EXERCISE and TIME did not reach statistical significance ($F_{(7.59, 68.33)} = 1.85$, $p = .087$), but the amplitude of the observed changes in movement time was comparable to the statistically significant differences (6 to 17 ms) observed between sessions in the current study and similar in effect size (0.21 to 0.54) to some of the larger exercise-induced effects observed in previous studies [120]. Before exercise began, movement time in the exercise session was shorter than before rest in the control session with mean differences of 5.4 ms for the simple reaction task, 7.7 ms for congruent flanker trials, and 7.3 ms for incongruent flanker trials. Within the exercise session, movement time decreased from minute 10 to minute 30 of exercise with mean decreases of 8.3 ms for the simple reaction task, 6.5 ms for congruent flanker trials, and 10.0 ms for incongruent flanker trials but then increased again at minute 0 after exercise (i.e., immediately after exercise) with mean increases of 11.2 ms for the simple reaction task, 7.6 ms for congruent flanker trials, and 10.8 ms for incongruent flanker trials. Conversely,

movement times at equivalent time points during the non-exercise control session never differed by more than 3 ms.

Reaction time

Figure 2.3 shows mean reaction time at all time points for all tasks in both sessions. Overall, reaction time differed across TASK ($F_{(8, 72)} = 4.46$, $p < .001$) with means of 365 ms for incongruent flanker trials, 335 ms for congruent flanker trials, and 279 ms for the simple reaction task. But there was an interaction between EXERCISE, TIME, and TASK ($F_{(12.51, 112.62)} = 2.78$, $p = .002$) so each level of TASK (i.e., incongruent flanker trials, congruent flanker trials, simple reaction task) was subsequently analyzed separately.

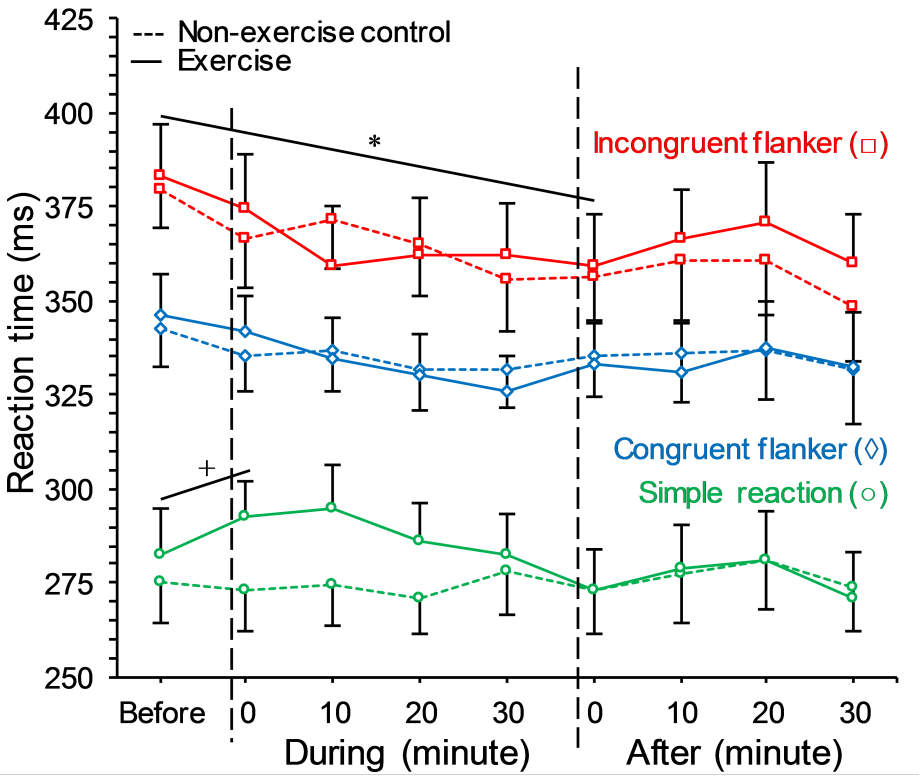

Figure 2.3. Reaction time (mean ± SEM) at each time point before, during, and after exercise or non-exercise control for simple reaction task, congruent flanker trials, and incongruent flanker trials. Exercise or non-exercise control is denoted by vertical dashed lines. In incongruent flanker trials, reaction time at minute 0 after exercise was significantly shorter than before exercise (* $p < .001$) but did not differ from non-exercise control. Simple reaction time at minute 0 of exercise was significantly longer than before exercise (+ $p = .025$).

For incongruent flanker trials, there was no effect of EXERCISE on reaction time ($F_{(1, 9)}$ = 0.35, p = .571) nor did EXERCISE interact with TIME ($F_{(6.60, 59.41)}$ = 1.34, p = .250); however, there was a main effect of TIME ($F_{(8, 72)}$ = 4.46, p < .001). When collapsed across sessions, mean reaction time decreased 23.6 ms from before to after exercise or non-exercise control ($t_{(19)}$ = 6.38, p < .001). Planned comparisons revealed that reaction time on incongruent flanker trials was not lower than control at minute 30 during exercise (one-tailed paired $t_{(9)}$ = -1.32, p = .905) or minute 0 after exercise (one-tailed paired $t_{(9)}$ = -0.57, p = .714).

For congruent flanker trials, reaction time was not influenced by EXERCISE ($F_{(1, 9)}$ = 0.01, p = .939), TIME ($F_{(4.04, 36.33)}$ = 1.88, p = .134), or an interaction between the two factors ($F_{(5.06, 45.50)}$ = 0.56, p = .730). Planned comparisons revealed that reaction time on congruent flanker trials was lower than control at minute 30 during exercise (5.6 ms, one-tailed paired $t_{(9)}$ = 1.25, p = .106) and minute 0 after exercise (2.0 ms, one-tailed paired $t_{(9)}$ = 0.45, p = .328) neither of these differences were statistically significant.

For the simple reaction task, EXERCISE interacted with TIME to influence reaction time ($F_{(8, 72)}$ = 4.07, p < .001). Reaction time was influenced by TIME in the exercise session ($F_{(8, 72)}$ = 5.80, p < .001): reaction time increased 11 ms from before exercise to minute 0 of exercise ($t_{(9)}$ = 2.26, p = .025) but was similar to before exercise again by minute 30 of exercise ($t_{(9)}$ = 0.09, p = .926). Reaction time was not influenced by time in the control session ($F_{(4,83, 43.50)}$ = 0.73, p = .604). Planned comparisons revealed that reaction time on the simple reaction task was not lower than control at minute 30 during exercise (one-tailed paired $t_{(9)}$ = -0.97, p = .833) or minute 0 after exercise (one-tailed paired $t_{(9)}$ = -0.03, p = .512).

Response accuracy (flanker task)

Response accuracy differed across TASK with means of 94.9 % in congruent trials and 77.9 % in incongruent trials ($F_{(1, 9)} = 24.79$, $p = .001$). TASK interacted with TIME to influence response accuracy ($F_{(5.66, 50.90)} = 2.69$, $p = .026$) but when each level of TASK was subsequently analyzed separately there was no significant influence of TIME on response accuracy for incongruent ($F_{(6.51, 58.62)} = 1.46$, $p = .194$) or congruent ($F_{(4.02, 36.17)} = 0.93$, $p = .449$) flanker trials. In incongruent flanker trials, there was a 9 % improvement in mean response accuracy from minute 30 of exercise to minute 0 after exercise (i.e., immediately following exercise); however, lack of statistically significant effects or interactions involving EXERCISE precluded further statistical analysis of this apparent improvement.

2.4 Discussion

This study set out to disentangle the influence of aerobic exercise on speed of processing and movement execution by partitioning response time into reaction time (i.e., before EMG onset) and movement time (i.e., after EMG onset), respectively, during simple reaction and flanker tasks. The present findings support the main hypothesis that a single session of aerobic exercise would have disparate effects on reaction time and movement time. As predicted, movement time was shorter near the end of the 40-minute exercise session than during the non-exercise control session for all tasks. Movement time then increased immediately after exercise for all tasks but remained lower than non-exercise control for the simple reaction task and incongruent flanker trials. Interestingly, movement time appeared to be shorter than the non-exercise control session before exercise began for all tasks and remained shorter than control until 10 to 20 minutes after exercise; however, these specific differences were not examined

statistically. Contrarily, reaction time during incongruent trials of the flanker task decreased over time but there were no consistent differences between the exercise and non-exercise control sessions. These findings demonstrate the importance of partitioning response time into reaction time and movement time when examining the influence of aerobic exercise on speed of processing.

Shortened movement time during aerobic exercise has previously been shown to coincide with an increase in early EMG activity[137,139] indicating recruitment of a greater number of motor units, which would produce greater force and contraction velocity causing the limb to move faster[172]. The potential mechanism underlying exercise's influence on movement time would therefore increase EMG activity (i.e., motor unit recruitment) without decreasing EMG latency (i.e., speed of processing). An increase in motor cortical or spinal excitability may increase EMG activity with little or no impact on EMG latency. Recent evidence shows that exercise influences the excitability of neurons in the primary motor cortex[173]. Transcranial magnetic stimulation (TMS) studies suggest that exercise suppresses inhibitory and facilitates excitatory intracortical networks that influence corticospinal tract output[174–177]. While exercise-induced modulation of these intracortical networks does not lead to a corresponding increase in corticospinal tract output after aerobic exercise[176,177] an increase in corticospinal tract output does occur alongside suppression of intracortical inhibition when measured between sets of an intermittent resistance exercise[174]. Therefore, during aerobic exercise, modulation of intracortical networks may enhance corticospinal tract output leading to increased EMG activity and the decrease in movement time observed in the current study; however, it is not currently known how the excitability of intracortical networks or the corticospinal tract are influenced during aerobic

exercise. A number of techniques, such as H-reflex and TMS, may be used in future research to localize the source of increased motor unit recruitment during exercise[178].

In addition to shortened movement time during exercise, the current study observed shorter movement time before exercise began compared to before the non-exercise control condition; it remained shorter than control throughout the exercise session until 10 to 20 minutes after exercise. Importantly, while the order of the exercise and control sessions were counter-balanced, each participant knew before each session whether they would be performing exercise. Therefore, it is possible that movement time was shortened by a mechanism that was activated in anticipation of exercise. There is currently no evidence in the TMS literature cited above that supports a modulation of motor cortex excitability prior to exercise because none of the cited studies included a non-exercise control group for comparison. One similar TMS study has reported no baseline differences between measures of corticospinal tract output or intracortical inhibition or facilitation before participants performed paired associative stimulation alone or in combination with exercise[179]. Some TMS studies have speculated that the neurotransmitter modulation hypothesized to link exercise to changes in cognition[141,142,180] may also contribute to the changes in motor cortical excitability observed after exercise[173,177]. Interestingly, plasma concentrations of norepinephrine and epinephrine may be elevated at rest in anticipation of exercise compared to rest when no exercise is forthcoming and these concentrations increase linearly with the relative intensity of the upcoming exercise[181]. However, at present, it remains unclear how these peripheral changes in plasma catecholamines relate to alteration of motor cortex excitability and movement time before or during aerobic exercise.

Contrary to our hypothesis, aerobic exercise did not decrease reaction time in the flanker task despite this task involving additional cognitive processes that may be selectively influenced

by aerobic exercise. Exercise-induced decreases in response time during speeded tasks have been purported to indicate an improvement in CNS speed of processing[63,120]. However, the present finding aligns with and extends recent research indicating that exercise-induced decreases in response time during speeded tasks can be attributed to a decrease in movement time (i.e., an increase in the speed of peripheral movement-related processes, which may still have a central origin), not reaction time[137–139] (i.e., CNS speed of processing). It would be premature to conclude that a single session of aerobic exercise does not confer any benefit to speed of processing but the current study further highlights the apparent importance of properly distinguishing reaction time (using EMG to indicate response onset) from movement time when examining speed of processing. Accordingly, previous studies purporting a beneficial effect of aerobic exercise on speed of processing need to be reassessed and interpreted with caution.

Further research is needed before the lack of an aerobic exercise-induced effect on speed of processing observed in the current study can be generalized beyond the specific cognitive processes, population, and exercise that have been examined. It is possible that exercise improves the speed of a process or processes not involved in these tasks. For example, response time decreases while performing visual search and sport-specific decision making tasks during exercise[182,183] but it is not known whether this exercise-induced reduction in response time reflects a reduction in movement time, reaction time, or both. Furthermore, while the EMG-based measure of reaction time is the gold standard and likely most specific and sensitive measure of overall CNS speed of processing, other measures may be more sensitive at determining the timing of specific cognitive processes. For example, electroencephalography studies examining the P3 event-related potential have shown that, under certain conditions, P3 latency decreases after an aerobic exercise session[100–102]. The P3 is thought to represent stimulus

evaluation time[184] so a reduction in P3 latency may represent an increase in the speed of that specific process.

The lack of an exercise-induced change in speed of processing in the current study may also be related to the age, health, and fitness of the sample tested. As with other measures of cognitive function[53,61,62], exercise-induced changes in speed of processing may be more pronounced, and easier to detect, in children, older adults, or people with CNS disease or injury whose speed of processing is initially slower. An individual's aerobic fitness also moderates the influence of a single session of exercise on cognition[121]. In the current study, participants' fitness ranged from poor (i.e., the lowest 4 to 11 %) to excellent (i.e., the highest 3 %) according to published age- and gender-specific normative data[171]. This wide range in fitness may have limited the observed effects.

Certain characteristics of exercise may also moderate any potential influence on speed of processing. We chose a single moderate intensity exercise session (i.e., 64 to 76 % HR_{max}) because it is shown to have the most robust influence on cognitive function[121]. Participants in our study exercised within this range at an average HR of 73.5 % of HR_{max} so the findings of this study may be specific to moderate intensity exercise. Changes in speed of processing may also be easier to detect after multiple aerobic exercise sessions. Speeded responses are faster in people who have been more active[111,185] or have trained aerobically[113] but how this change accrues over multiple aerobic exercise sessions remains unclear. The contributions of movement speed and speed of processing to these longer-term changes in response speed are also not fully understood.

A final possibility, and a limitation of this study, is that a learning effect may have confounded any observable influence that aerobic exercise had on speed of processing. In both

sessions, exercise and control, reaction time during incongruent flanker trials decreased over the first 3 to 5 blocks (i.e., 180 to 300 trials) before plateauing. There was no apparent change in accuracy over these blocks; however, there was an apparent, but not statistically significant, increase in accuracy during the exercise session immediately after exercise was completed. It is possible that learning during incongruent trials of the flanker task occurs in the form of an increase in speed of processing followed by an increase in accuracy. Aerobic exercise may influence the timing and magnitude of this learning process; however, the lack of statistical significance in the current study makes it impossible to determine the relationship between aerobic exercise and learning during this task. Future research should examine the influence of aerobic exercise on learning during incongruent trials of the flanker task. Studies interested in examining the influence of aerobic exercise on the flanker task separate from learning should be sure to allow 200 to 300 trials of practice at the beginning of each session.

In the current study, we observed an increase in simple reaction time during exercise, which may represent a dual-task effect of combining aerobic exercise with a secondary cognitive task[186]. At the start of exercise, simple reaction time was longer than before exercise. This fits with previous research indicating that simple reaction time is longer during short sessions of cycling exercise at a constant load[187]. This longer reaction time likely represents the attentional demands of exercise. Interestingly, in our study, by the end of exercise simple reaction time was not longer than before exercise. In the previously mentioned study, they found a parabolic relationship between reaction time and pedal rate. At a constant load, reaction times were quickest at the pedal rate that was also the most energy efficient (i.e., had the lowest VO_2) and were not significantly higher at a freely chosen rate indicating that these pedal rates require the least amount of attention. In our study, participants were allowed to freely choose the pedal rate

throughout a much longer exercise session. Chosen pedal rate while performing the cognitive tasks did not change over the course of the exercise session but it is possible that the most energy efficient pedal rate became closer to the freely chosen actual pedal rate leading to a decrease in the attention required and an improvement in simple reaction time. The dual-task paradigm assumes that priority is given to the primary task, in this case exercise, to ensure that performance does not decrease. Interestingly, participants in the current study pedalled faster while performing the cognitive task than they did during exercise alone. While this may seem to indicate an improvement or at least maintenance of exercise performance it may indicate a shift of attention away from exercise.

2.5 Conclusions

This study revealed that a single session of aerobic exercise speeds up movement execution (movement time) but not CNS processing (reaction time). This work reinforces the importance of partitioning response time into premotor and motor components representing reaction time and movement time, which can be achieved using EMG. It is recommended that this technique be used in future research examining speed of processing in response to both a single session of aerobic exercise and long-term aerobic training or fitness. Additionally, reaction time during incongruent flanker trials decreased over time with or without aerobic exercise indicating that caution should be taken when interpreting pre-to-post exercise changes in behaviour. Future research should attempt to control this decrease in reaction time to determine whether it is masking a potential effect of aerobic exercise.

Chapter 3: Study 2

Error-related conflict after a single aerobic exercise session

3.1 Introduction

Cognitive control is associated with a wide range of measures of real-life function including mental health, physical health, quality of life, school success, work success, marital harmony, and public safety (Diamond, 2013). Inhibitory control is one important executive function that allows the selective suppression of compelling, but unwanted, attention, thought, emotion, and behaviour in order to bias the performance of behaviour that aligns with internally-held goals or intentions instead of other conflicting behaviour[2–4]. Inhibitory control declines with age and is impaired in various mental health disorders (Diamond, 2013). Conversely, cognitive functions can benefit from long- and short-term aerobic exercise[53,54,63,105,106,119–121]. It is noteworthy that cognitive control functions, such as inhibitory control, may enjoy selectively greater benefits from exercise[61,62]. In the current study, we examine the influence of a single session of aerobic exercise on behavioural and electrophysiological measures of conflict associated with inhibitory control during a flanker task.

Inhibitory control and related cognitive functions are often examined during a modified Eriksen flanker task[75,87]. During a flanker task, the performer must make a choice response to a central target stimulus while disregarding irrelevant stimuli that flank the target. These flanker stimuli create interference or conflict particularly when they indicate a response that is incongruent with the target stimulus[74,75,87]. Inhibitory control allows performers of the flanker task to reduce this conflict by selectively attending to the relevant central target stimulus while

suppressing attention to the compelling but irrelevant flanker stimuli and inhibiting the predisposed response driven by them.

The conflict created by incongruent flanker stimuli influences behavioural measures of task performance as well as electrophysiological measures of underlying brain activity. Behavioural measures of performance (e.g., reaction time, response accuracy) are often used to index the interference or conflict created by flanker stimuli in the incongruent condition (i.e., flankers indicate a different response than the target) relative to the congruent condition (i.e., flankers indicate the same response as the target) or a neutral condition (i.e., flankers do not indicate a response). When performing the flanker task, mean reaction time is longer and response accuracy is lower during incongruent than congruent or neutral trials[75,97], which is often quantified by calculating the flanker interference effect, the difference in mean reaction time or response accuracy between congruent and incongruent trials.

These behavioural indices of the interference or conflict caused by incongruent flanker stimuli are supported by electrophysiological evidence. The P3 is a stimulus-locked electroencephalography (EEG) event-related potential (ERP) component that is thought to represent attention and memory-related processing of a stimulus in order to update the representation of that stimulus within the context of the ongoing task[98,99]. When performing the flanker task, mean P3 amplitude is lower and mean P3 latency is longer during incongruent trials compared to congruent trials[64,65,100–102]. As with the above behavioural measures, these congruency-dependent differences in the P3 may be interpreted as an indication of the higher cognitive demand of performing incongruent trials due to the conflict created by the flanker stimuli.

Conflict created by the incongruent flankers can also be indexed by measuring electrophysiological activity related to conflict monitoring. The error-related negativity (ERN) is a response-locked EEG ERP component that accompanies errors during speeded responses[103,104] such as those committed during incongruent trials of the flanker task. The generator of the ERN has been localized to the anterior cingulate cortex (ACC)[188,189]. High ACC activity during errors is related to the high level of conflict that led to the error, rather than the commission of the error itself so the ERN is thought to represent this ACC conflict-monitoring activity[83,86].

As noted, many cognitive functions benefit from long- and short-term aerobic exercise but inhibitory control may enjoy a selectively greater improvement[53,54,61–63,105,106,119–121]. Improvements in behavioural and electrophysiological measures during the flanker task occur after a single session of aerobic exercise regardless of flanker congruence; however, aerobic exercise often has a greater influence during incongruent trials compared to congruent or neutral trials. Response time decreases after aerobic exercise regardless of flanker congruence[101,102]. As well, P3 amplitude increases[64,65,100–102] and P3 latency decreases[102] after exercise regardless of flanker congruence. However, some studies have shown a greater response time decrease during incongruent trials indicated by a decrease in the flanker interference effect[64,65] or an interaction between exercise and flanker congruence[64]. P3 latency also decreases more during incongruent flanker trials[100,101]. Because these behavioral and electrophysiological differences between congruent and incongruent trials are thought to represent the conflict or interference created by incongruent flankers, it follows that this selective effect of aerobic exercise on incongruent flanker trials represents a reduction in this conflict, possibly due to an improvement in inhibitory control.

Presumably, if changes in behaviour during the flanker task following aerobic exercise are attributable to a reduction in conflict they may be detectable in the ERN. Only one previous study has examined the ERN following a single session of aerobic exercise but did not find an effect of exercise[135]. However, they performed the flanker task after heart rate returned to within 10% of baseline, which they reported as a mean (sd) time of 40.1 (13.9) minutes while a meta-analysis has shown that the greatest positive effects of exercise occur within 15 minutes of cessation[121]. As a result, the current study re-examined the influence of a single session of aerobic exercise on behavioural and electrophysiological measures of conflict associated with inhibitory control during a flanker task. Our primary purpose was to examine whether exercise-related changes in behaviour and electrophysiology that have been attributed to a reduction in conflict could be observed in an EEG measure of conflict-related brain activity, the ERN. As such, we hypothesized that immediately after exercise there would be a reduction in ERN amplitude compared to before exercise. Furthermore, we predicted that this reduction in ERN amplitude would coincide with previously observed behavioural and electrophysiological indications of reduced conflict. Specifically, we hypothesized that immediately after exercise, reaction time and P3 latency would be shorter and P3 amplitude would be larger compared to before exercise regardless of flanker congruency but the effect of aerobic exercise on reaction time and P3 latency would be greater for incongruent than congruent trials. Revealing the influence of a single session of aerobic exercise on conflict-related brain activity is an important step in understanding how aerobic exercise benefits cognitive control and overall cognitive function.

3.2 Methods

Participants

Sixteen healthy, young adults (8 female) volunteered to participate in this study. This study was approved by the Office of Research Ethics at the University of Waterloo and all participants provided written informed consent before participating. Participants were screened for exclusion criteria including musculoskeletal or neurologic disorders that may have affected their ability to perform the study and their readiness to exercise without requiring permission from their physician (Physical Activity Readiness Questionnaire, Canadian Society for Exercise Physiology, Ottawa, ON).

Experimental protocol

Each participant volunteered to visit the laboratory for three separate sessions: 1) screening and graded exercise test, 2) exercise session, and 3) non-exercise control session. The first session preceded the second session by 2-17 days; the second and third session were 2-7 days apart. All three sessions were performed at the same time of day for each participant. The order of the last two sessions and time-of-day of both sessions were counter-balanced across participants.

Upon arrival for the first session, participants were provided information about the study before consenting to participate. During this initial session, participants received instruction and familiarization with the Borg Rating of Perceived Exertion (RPE) and the magnetic-resistance recumbent cycle ergometer that was used throughout the experiment. Participants then performed the graded exercise test (GXT) to establish aerobic fitness levels and determine the work rate for the exercise session.

Participants started both experimental sessions (exercise and non-exercise) seated in a chair in front of a computer monitor. After sitting quietly for two minutes while resting heart rate was measured participants performed four 100-trial blocks of the flanker task for practice. After a four-minute break, participants then performed five more blocks of the flanker task before being seated on the cycle ergometer. In the exercise session, participants were then allowed five minutes to warm up before exercising for 30 minutes. In the non-exercise control session, participants sat quietly on the recumbent cycle ergometer for 35 minutes without pedalling. Immediately after exercise or non-exercise control participants returned to the chair in front of the computer monitor to perform five more blocks of the flanker task.

Graded exercise test

Each participant performed a GXT on the cycle ergometer to measure peak oxygen consumption (VO_2peak) and determine the work rate for the experimental exercise session. Before starting the test, participants rested quietly for 2 minutes. The test started with the participant pedaling at a rate greater than 55 revolutions per minute (RPM) at effort level 3. Every two minutes the effort level was increased by 4 until the participant chose to stop or could no longer maintain a pedal rate of 55 RPM. Effort levels on the cycle ergometer were chosen to start at a power of 50 W while pedaling at 55 RPM and increase 50 W every two minutes if the same pedal rate is maintained.

Throughout the test, respiratory gases were analyzed breath-by-breath (Vmax 229, SensorMedics Inc., Palms Springs, CA) and electrocardiogram (ECG; EK-10, Burdick Inc., Milton, WI) was measured continuously. Gas analysis and ECG were transmitted to computer software (Vmax Vision, SensorMedics Inc., Palms Springs, CA) for calculation of variables of

interest [e.g., oxygen consumption (VO_2), respiratory exchange ratio (RER), and heart rate (HR)]. These variables were displayed in real-time and stored for offline processing and analysis. RPE was measured at the beginning of each work level. Offline, VO_2, RER, and HR were averaged over 20-second intervals. Resting VO_2 was the mean VO_2 during the 2-minute rest period prior to exercise. VO_{2peak}, RER_{peak}, RPE_{peak}, and HR_{peak} were calculated as the respective peaks achieved during the GXT. Oxygen uptake reserve (VO_2R) was calculated as the difference between VO_{2peak} and resting VO_2.

GXT results were compared to commonly used pre-determined criteria [169] to test whether each participant achieved a true VO_{2peak}. The primary criterion was an increase in VO_2 of less than or equal to 2.1 ml/kg/min after an increase in workload. Secondary criteria were a RER_{peak} greater than 1.1, RPE_{peak} greater than 9, HR_{peak} greater than 90% of age-predicted (i.e., 220 – age). To be deemed a true VO_{2peak} the primary criterion or at least two of the secondary criteria must have been achieved during the test.

Exercise and associated measures

During the experimental exercise session, each participant performed a 30-minute session of exercise on a magnetic-resistance recumbent cycle ergometer (Excite 700iP, Technogym, Fairfield, NJ). Exercise intensity was set and monitored using the work level, RPE, and HR coinciding with 40-59% VO_2R during the participant's GXT. Throughout the warm-up and exercise participants pedalled at a self-selected comfortable rate while the work level was adjusted by the researcher to maintain the desired intensity. Each participant began the 5-minute warm-up pedaling at work level 3 while the researcher gradually increased the work level to that coinciding with 40% VO_2R. During the 30-minute exercise session participants continued to

pedal at a self-selected comfortable rate while the researcher adjusted the work level to maintain a HR in the range coinciding with 40-59% VO_2R. A switch on the cycle ergometer indicated each revolution of the pedals and was used to calculate pedal rate.

Electrocardiography. For the GXT, exercise, and non-exercise control sessions ECG was collected continuously (EK-10, Burdick Inc., Milton, WI). Electrodes were placed at the center of the manubrium and bilaterally over the 5th intercostal space along the mid-clavicular line. Data were sampled at 1,000 Hz and stored for offline processing. ECG was used to calculate heart rate (HR) in beats per minute (BPM). During exercise, a real-time heart rate was calculated and displayed to monitor exercise intensity.

Borg Rating of Perceived Exertion. RPE[170] was used to monitor exercise intensity. Throughout the graded exercise test and exercise session, the participant was asked to verbally rate their perceived exertion on a scale from 0 (nothing at all) to 10 (very, very strong).

Flanker task and associated measures

Before and after exercise or non-exercise control, participants sat in a chair in front of a computer monitor to perform a modified flanker task[75,102] delivered via custom software (LabVIEW, National Instruments, Austin, TX). Participants fixated on a point in the center of the stimulus presentation display. They began each trial with their hands supported prone on a table in front of them, each thumb resting on a button. In each trial a target stimulus was presented consisting of a right or left pointing arrow (i.e., > or <). The target stimulus was flanked by 4 additional arrows, two on each side, that were either congruent (< < < < < or > > > > >) or incongruent (< < > < < or > > < > >) with the target arrow. Participants responded by pressing a button with their right or left thumb as quickly as possible as indicated by the target

arrow. A stimulus was presented for 100ms every 2 seconds and participants were allowed 1500ms to respond. In each block, 25 stimuli of each condition were presented in random order for a total of 100 trials. A voltage output indicating whether the button was pressed or not was sampled at 1,000 Hz and stored for offline processing.

Electromyography. Reaction time was determined from the onset of muscle activity preceding a button press with the thumb. Bilateral flexor pollicis brevis electromyography (EMG) was measured to determine the onset of muscle activity. Electrodes were placed on the muscle belly bilaterally and another electrode was placed on the left ulnar styloid process to act as a ground. Data were amplified (x 500), filtered (10 to 1,000 Hz) (AMT-8, Bortec Biomedical, Calgary, AB), sampled (1,000 Hz), and stored for offline processing.

Electroencephalography. To record brain activity, EEG was recorded from 30 channels using Ag/AgCl electrodes arranged according to the International 10-20 system [190] and embedded into a Lycra cap (Quik-Cap, Compumedics Neuroscan, Charlotte, NC). To record eye movements and blinks, electrooculography (EOG) was recorded using Ag/AgCl electrodes placed above and below the left eye and lateral to the outer canthus of both eyes. For both EEG and EOG, an electrode at AFz was used as a ground and all electrodes were referenced to the average activity of electrodes located over the left and right mastoid. Impedances for all electrodes were below 5 kΩ. For each block of flanker trials, continuous EEG was amplified (x 19), filtered (DC to 300 Hz), and sampled (1000 Hz) using a Neuroscan amplifier (NuAmps, Compumedics Neuroscan, Charlotte, NC) and software (Scan, Compumedics Neuroscan, Charlotte, NC).

Data processing

EMG signals were bandpass filtered (20-500 Hz), baseline corrected, and full-wave rectified (FWR EMG) before being low-pass filtered (50 Hz; smoothed EMG). FWR and smoothed EMG were used to determine flexor pollicis brevis muscle activity onset using the following criteria: 1) FWR and smoothed EMG must both exceed a threshold equal to the mean plus 3 standard deviations of a 100-ms pre-stimulus baseline and 2) smoothed EMG must remain above this threshold for at least 25 ms.

Each trial was assigned a response status based on the muscle activity and button press response to the stimulus as follows: 'no response' when neither button was pressed, 'correct response' when only the correct button was pressed, 'incorrect response' when only the incorrect button was pressed, 'remedial response' when the incorrect button was pressed followed by the correct button, 'partial incorrect response' when muscle activity on the incorrect side preceded a correct button press, and 'undefined' for any other combination of button presses.

Accuracy was calculated based on button press only and is therefore expressed as the percentage of correct and partial incorrect responses relative to the total number of responses. Reaction time and movement time were calculated for correct responses only. Reaction time was the time between stimulus onset and muscle activity onset. Movement time was the time between muscle activity onset and response completion (i.e., button press).

EEG data were band-pass filtered (1 to 100 Hz). Epochs were extracted around the onset of each flanker stimulus (-1000 to 1750 ms) and baseline corrected (-500 to -400 ms). Each epoch was visually inspected and rejected if electrodes contained large amplitude voltage changes indicating noise other than eye artifact. ICA was then performed using the extended Infomax algorithm [191]. Independent components were visually inspected and those representing

eye and muscle artifact were removed. Each epoch was visually inspected again for additional noise removal. Electrode voltages were compared to independent component activations to determine if remaining noise could be removed by epoch rejection or independent component rejection. Separate stimulus- and response-locked epochs were then created to examine ERP components of interest.

P3 was examined on trials with a correct response at electrode Pz. Epochs were low-pass filtered (30 Hz) and epochs were extracted around the onset of each flanker stimulus (-1000 to 1000 ms). Separate ERPs were created for congruent and incongruent trials before and after exercise and non-exercise control by averaging all epochs at each time point. Within each ERP, P3 peak was the highest amplitude positive peak between 300 and 650 ms after stimulus onset. P3 amplitude was the voltage difference between the P3 peak and a 200-ms baseline starting 700 ms before stimulus onset. P3 latency was the time from stimulus onset to P3 peak.

ERN was examined at electrode FCz in 10 participants that made at least five remedial responses[192,193] in each block (i.e., before and after both interventions). Only remedial trials were used as error trials as we wanted to be sure that participants knew they had committed an error. Epochs corresponding to incongruent trials with a remedial response were low-pass filtered (15 Hz) and epochs were extracted around incorrect side EMG onset (-1000 to 1000 ms). Separate ERPs were created for remedial trials before and after exercise and non-exercise control by averaging all epochs at each time point. Within each ERP, ERN peak was the highest amplitude negative peak between 1 and 200 ms after EMG onset. ERN amplitude was the voltage difference between the ERN peak and a 100-ms baseline starting 1000 ms before EMG onset. ERN latency was the time from EMG onset to ERN peak.

Statistical analysis

Correct and error trials with a reaction time to the first button press lower than 150 ms or higher than 1000 ms were deemed unlikely to represent true reaction time and were removed from all behavioural and EEG analysis. The influence of flanker congruence, time, and exercise on response accuracy, reaction time, and movement time was determined using separate repeated-measures analyses of variance (ANOVA) with three factors: CONGRUENCE (2 levels: congruent and incongruent), EXERCISE (2 levels: exercise and non-exercise control), and TIME (2 levels: before or after exercise or control). P3 amplitude and latency were also analyzed using separate repeated measures ANOVAs with CONGRUENCE, EXERCISE, and TIME as factors. ERN amplitude and latency were analyzed using separate repeated measures ANOVAs with only EXERCISE and TIME as factors. Post hoc analyses of significant interactions and main effects in omnibus ANOVAs were performed using t-test. An alpha level of $p <= .05$ was used to denote statistical significance.

3.3 Results

Participant demographic, fitness, and exercise characteristics

Sixteen young healthy adults [8 female; mean (sd) age 24.0 (4.3) years] volunteered to participate in the study. Individual and group mean demographic and GXT data are shown in Table 3.1. Males and females are separated to permit comparisons against normative data. During the GXT, all participants achieved the predetermined criteria for VO_{2peak}. Fitness was assessed by comparing VO_{2peak} to published normative data based on age and gender [171]. The group mean VO_{2peak} was 41.6 (6.1) ml/kg/min, which would be in the fair to good normative groups depending on age and gender. During the exercise session, participants exercised at a

mean HR of 75.5 (5.2) % of HR_{peak} and a mean RPE of 3.90 (1.20), which were both within the mean target ranges of 67.4 to 78.2 % and 2.63 to 4.91, respectively (Table 3.2). The 10 participants that made at least five remedial responses in each block (i.e., before and after both interventions), qualifying them for ERN analysis[192,193], are denoted in bold in Tables 3.1 and 3.2.

Table 3.1. Individual participant demographic and graded exercise test data.

	Demographic				Graded Exercise Test		
ID	Sex	Age (years)	Height (cm)	Weight (kg)	Peak HR (BPM)	Peak VO2 (ml/kg/min)	VO2 norm group
Females							
1	**F**	**20**	**175**	**69**	**181**	**36.4**	**Fair**
2	F	23	167	60	177	37.1	Average
4	**F**	**29**	**172**	**77**	**177**	**33.6**	**Fair**
8	**F**	**20**	**163**	**70**	**175**	**41.7**	**Average**
10	**F**	**21**	**160**	**71**	**182**	**35.1**	**Fair**
11	F	25	165	62	194	39.4	Average
12	**F**	**18**	**168**	**68**	**196**	**34.8**	**Fair**
15	F	33	172	65	186	38.0	Good
Males							
3	**M**	**25**	**185**	**76**	**186**	**48.3**	**Good**
5	**M**	**19**	**185**	**79**	**180**	**52.7**	**Good**
6	M	25	185	83	206	53.2	Good
7	**M**	**21**	**167**	**73**	**179**	**45.0**	**Average**
9	**M**	**23**	**167**	**62**	**183**	**45.1**	**Average**
13	**M**	**24**	**190**	**101**	**179**	**43.6**	**Average**
14	M	30	172	86	191	41.8	Average
16	M	28	175	87	178	40.0	Fair
Mean		24.0	173.0	74.3	184.4	41.6	
SD		4.3	8.9	11.0	8.5	6.1	

HR = heart rate, VO2 = volume of oxygen consumed. VO2 norm groups are from Shvartz & Reibold, 1990. Bolded participants committed enough errors for ERN analysis.

Table 3.2. Individual exercise characteristics.

	Target HR (% peak)		HR (% peak)		Target RPE		RPE		Work level		Pedal rate (RPM)	
ID	Min	Max	Mean	SD	Min	Max	Mean	SD	Mean	SD	Mean	SD
1	**73.5**	**84.5**	**87.0**	**2.9**	**2.5**	**4.5**	**4.43**	**0.73**	**6.3**	**1.0**	**61.2**	**2.9**
2	72.9	82.5	80.4	2.9	1.5	3.0	1.86	0.38	5.8	0.4	50.4	3.5
3	**65.1**	**75.8**	**73.8**	**3.0**	**2.0**	**4.5**	**3.00**	**0.00**	**9.0**	**1.4**	**63.7**	**1.7**
4	**74.0**	**82.5**	**76.9**	**2.5**	**2.5**	**4.5**	**3.86**	**0.90**	**7.8**	**0.8**	**59.7**	**1.1**
5	**63.9**	**76.1**	**75.4**	**2.6**	**2.5**	**5.0**	**5.43**	**1.13**	**11.7**	**0.8**	**64.2**	**4.4**
6	56.8	68.9	74.6	5.6	3.0	6.0	4.00	0.58	16.3	0.8	55.8	1.9
7	**65.4**	**75.4**	**77.4**	**3.9**	**2.0**	**4.5**	**3.57**	**0.45**	**7.5**	**1.8**	**64.5**	**6.9**
8	**66.3**	**77.1**	**73.0**	**3.5**	**2.5**	**5.0**	**4.29**	**1.50**	**4.8**	**1.3**	**72.5**	**3.1**
9	**70.5**	**82.0**	**81.2**	**3.0**	**4.0**	**6.0**	**4.14**	**0.38**	**6.0**	**1.7**	**62.3**	**1.7**
10	**70.9**	**80.2**	**74.8**	**2.2**	**2.0**	**4.0**	**2.29**	**0.76**	**4.2**	**0.8**	**69.9**	**1.9**
11	68.0	77.3	71.8	2.2	1.5	2.5	3.14	0.69	6.3	0.5	63.9	2.7
12	**72.5**	**81.6**	**75.9**	**1.8**	**2.0**	**4.5**	**2.64**	**0.48**	**6.0**	**0.0**	**49.9**	**1.5**
13	**66.5**	**78.8**	**69.6**	**5.0**	**3.5**	**6.5**	**4.57**	**1.27**	**11.5**	**0.8**	**59.1**	**2.2**
14	57.6	71.2	66.1	5.1	4.0	6.5	6.57	2.07	10.8	1.2	57.1	4.9
15	72.0	83.3	80.9	2.3	2.5	5.0	3.57	0.79	6.0	1.3	65.6	3.4
16	62.9	73.6	69.1	2.3	4.0	6.5	5.07	0.79	7.0	0.0	69.6	1.2
Mean	67.4	78.2	75.5		2.6	4.9	3.90		8.0		61.8	
SD	5.4	4.5	5.2		0.9	1.2	1.20		3.2		6.4	

HR = heart rate, RPE = rate of perceived exertion, RPM = revolutions per minute. Bolded participants committed enough errors for ERN analysis

ERN amplitude and latency

Grand-average (N = 10, subjects who committed enough errors for ERN analysis) response-locked ERPs showing the ERN at FCz electrode site are presented in Figure 3.1. Overall, there were no differences in ERN latency and amplitude comparing task conditions. Mean ERN peak amplitude, across all conditions, was -5.71 (5.98) μV and was not influenced by TIME or EXERCISE (all $F < 0.32$, all $p > .588$, Figure 3.2A). Contrary to our hypothesis, ERN increased 0.13 μV from before to after exercise, but this increase was not analyzed due to a lack

of main effects or interactions. Mean ERN peak latency was 125.1 (28.9) ms and was also not influenced by TIME or EXERCISE (all $F < 1.18$, all $p > .305$, Figure 3.2B).

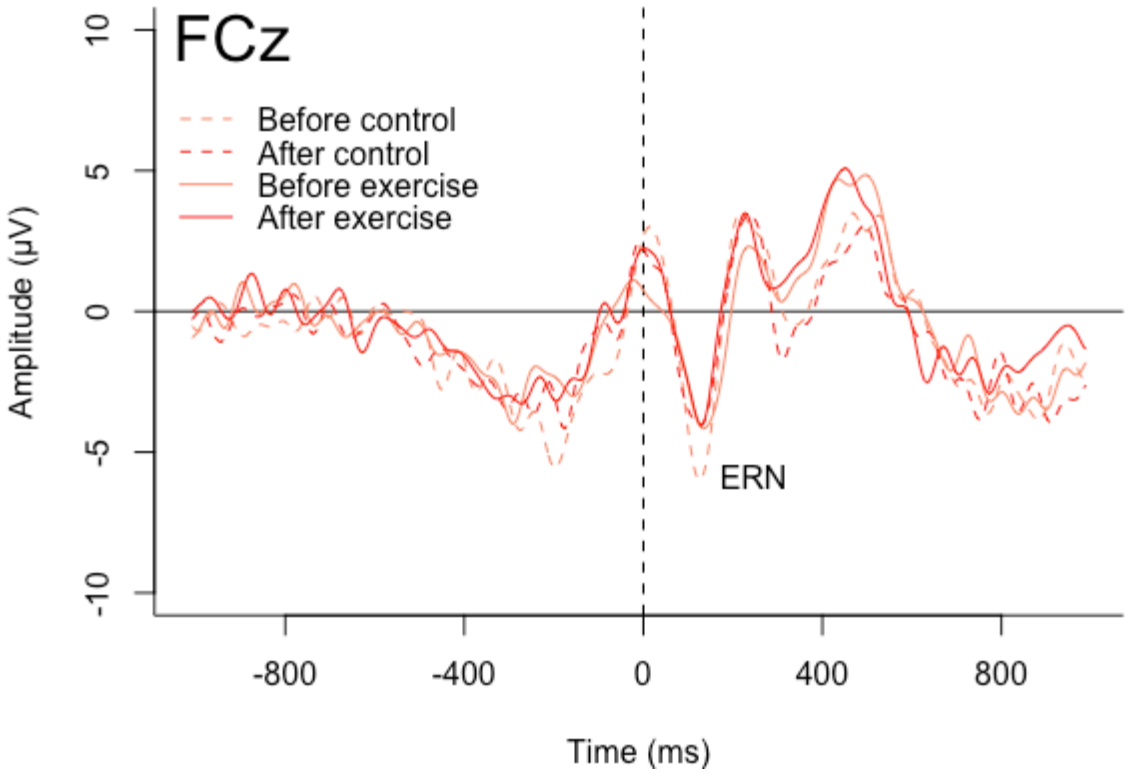

Figure 3.1. Response-locked (i.e., EMG onset) ERP showing the ERN on incongruent flanker trials before and after exercise and non-exercise control. ERP is the grand average at FCz electrode site of all participants with at least 5 remedial trials in all conditions (N = 10). EMG onset is denoted by the vertical dashed line at time 0.

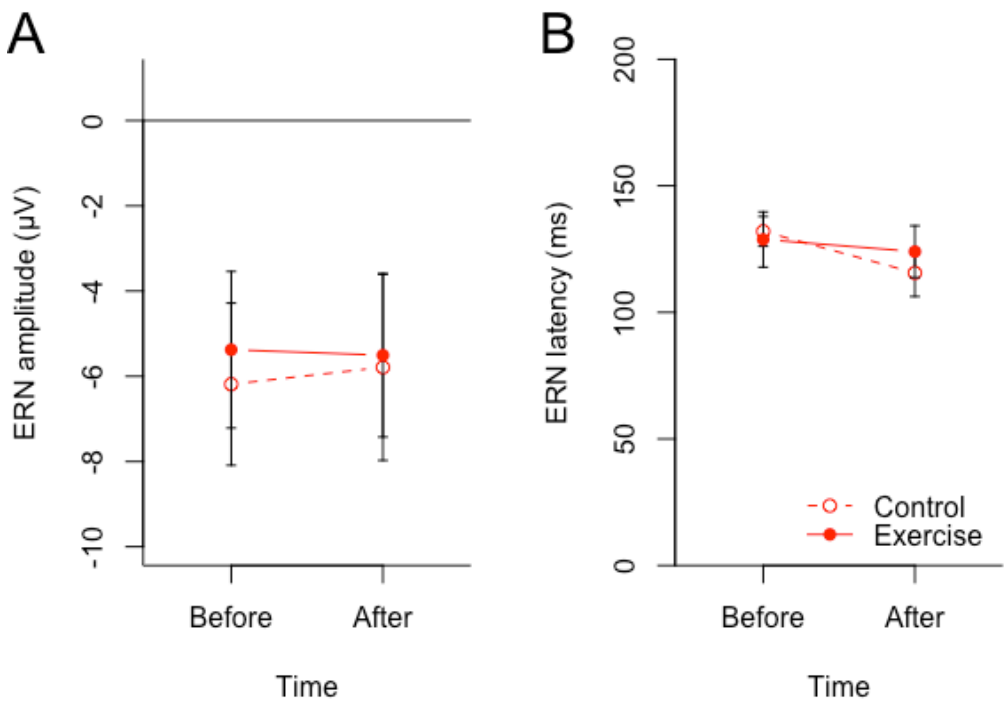

Figure 3.2. ERN amplitude (mean ± SEM, A) and latency (B) before and after exercise and non-exercise control.

P3 amplitude and latency

Grand-average stimulus-locked ERPs showing the P3 at Pz electrode site are presented in Figure 3.3. Overall, both P3 amplitude and latency differed as expected by congruency but were not influenced by any other conditions. P3 peak amplitude (Figure 3.4A) was 1.14 μV higher on congruent than incongruent flanker trials [9.35 (3.61) vs. 8.21 (3.02) μV, $F_{(1, 15)} = 28.97$, $p < .001$, Figure 3.4B]. P3 peak amplitude was not influenced by TIME or EXERCISE nor were there any interactions between factors (all $F < 1.58$, all $p > .228$). P3 peak latency (Figure 3.5A) was 30.6 ms shorter on congruent than incongruent flanker trials [406.8 (52.1) vs. 436.3 (70.0) ms, $F_{(1, 15)} = 23.40$, $p < .001$]. TIME and CONGRUENCE interacted to influence P3 peak latency ($F_{(1, 15)} = 5.84$, $p = .029$). Post hoc analysis revealed that P3 peak latency was 34.5 ms shorter on congruent than incongruent flanker trials before the intervention [406.9 (51.3) vs. 441.4 (67.7) ms, $t_{(15)} = 5.20$, $p < .001$] but only 24.5 ms shorter after the intervention [406.8 (53.6) vs. 431.3

(72.9) ms, $t_{(15)} = 3.93$, $p = .001$]; although, both differences were statistically significant (Figure 3.5B). P3 peak latency on incongruent trials decreased 10.1 ms from before to after the intervention (i.e., exercise and control sessions collapsed); however, this decrease was not statistically significance [441.4 (67.7) vs. 431.3 (72.9) ms, $t_{(15)} = 1.18$, $p = .256$]. P3 peak latency was not influenced by EXERCISE [$F_{(1, 15)} = 2.72$, $p = .120$].

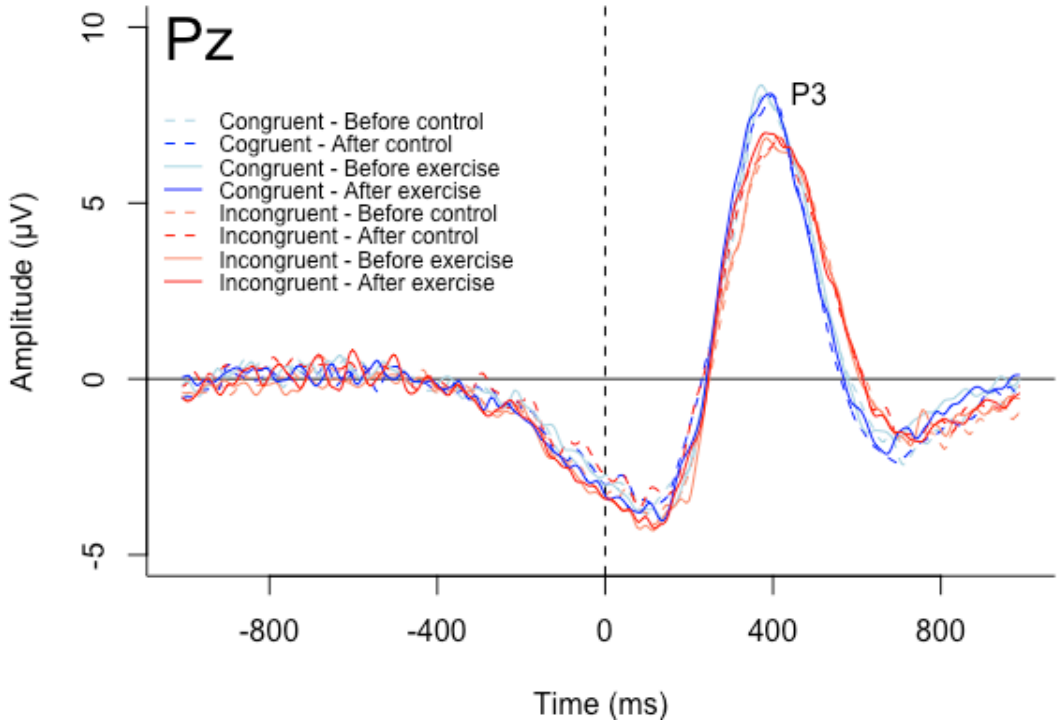

Figure 3.3. Stimulus-locked ERP showing the P3 on congruent and incongruent flanker trials before and after exercise and non-exercise control. ERP is the grand average at Pz electrode site of all participants (N = 16). Stimulus onset is denoted by the vertical dashed line at time 0.

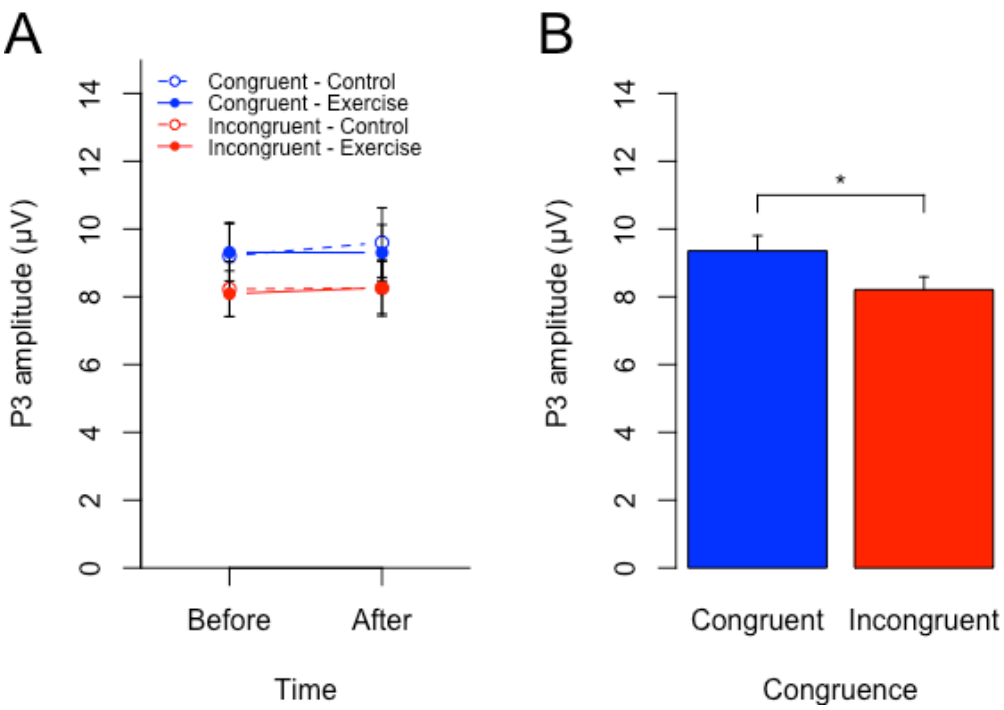

Figure 3.4. P3 amplitude (mean ± SEM) on congruent and incongruent flanker trials before and after exercise and non-exercise control (A). P3 amplitude on incongruent trials was significantly lower than on congruent trials (* $p <$ .001, B).

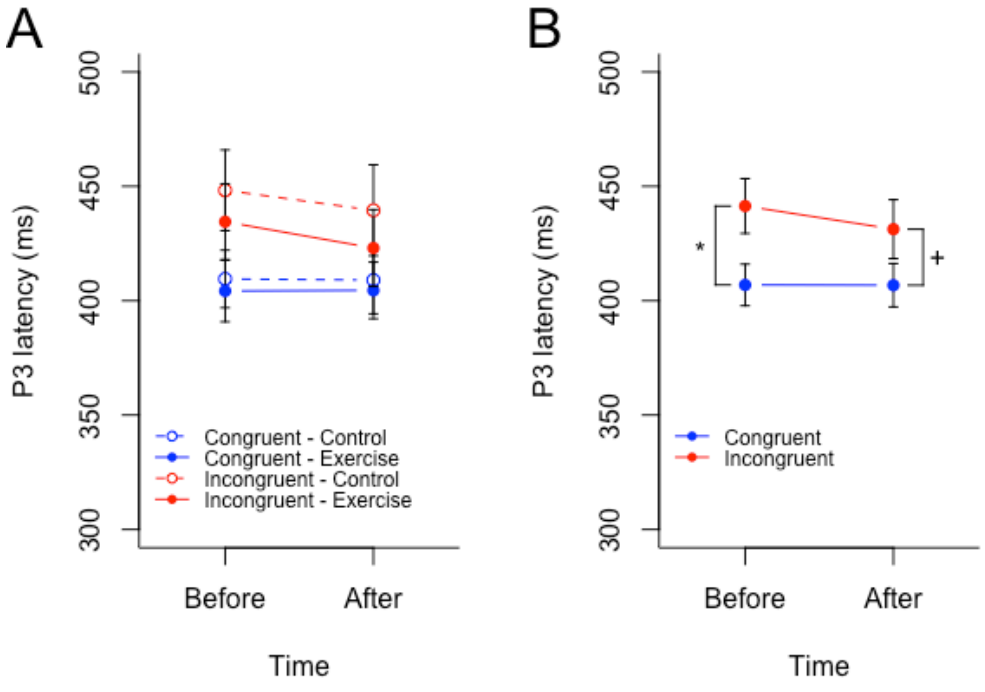

Figure 3.5. P3 latency (mean ± SEM) on congruent and incongruent flanker trials before and after exercise and non-exercise control (A). P3 latency on incongruent trials was significantly longer than on congruent trials both before (* $p <$ .001) and after (+ $p =$ .001) the intervention (i.e., exercise and non-exercise control collapsed, B).

Reaction time

Reaction time (Figure 3.6A) was 21.2 ms shorter on congruent than incongruent flanker trials [311.8 (31.3) vs. 333.0 (38.0) ms, $F_{(1, 15)} = 65.14$, $p < .001$, Figure 3.6B]. Reaction time also decreased 5.5 ms from before to after the intervention (i.e., exercise and control sessions collapsed); however, this decrease did not reach statistical significance [325.1 (38.2) vs. 319.6 (34.2) ms, $F_{(1, 15)} = 4.35$, $p = .055$]. Reaction time was not influenced by EXERCISE ($F_{(1, 15)} = 0.00$, $p = .963$).

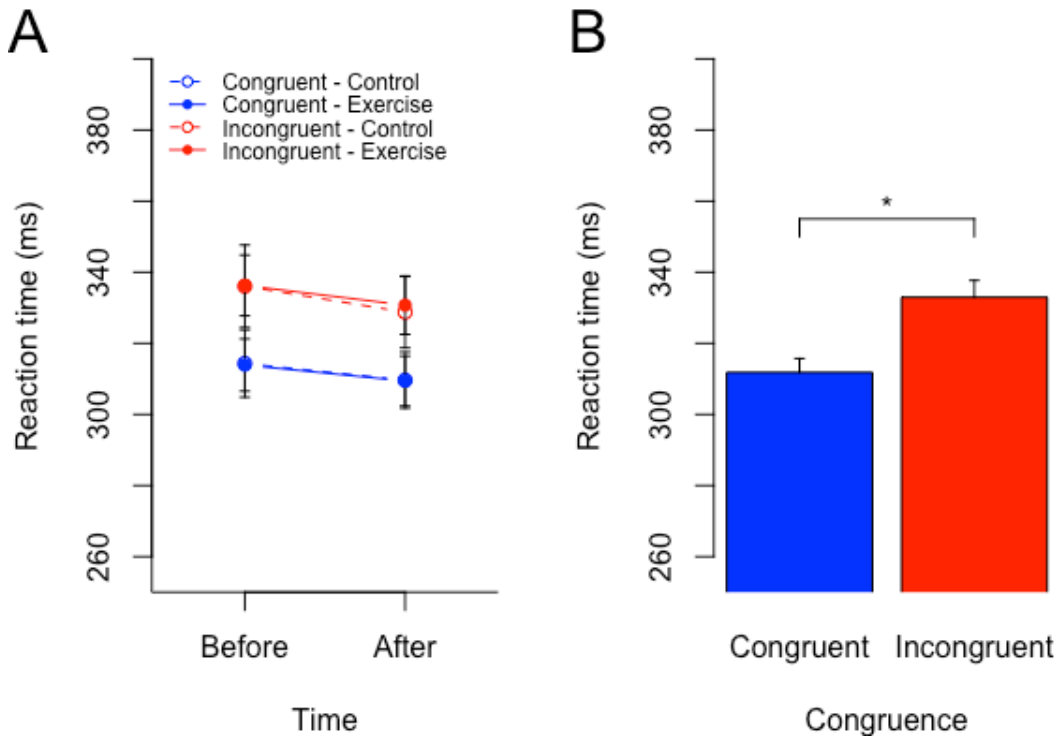

Figure 3.6. Reaction time (mean ± SEM) on congruent and incongruent flanker trials before and after exercise and non-exercise control (A). Reaction time on incongruent trials was significantly longer than on congruent trials (* $p <$ .001, B).

Movement time

Movement time, averaged across all sessions, task conditions, and time points, was 83.2 (16.4) ms. Movement time decreased 2.7 ms from before to after exercise but only 1.4 ms from

before to after non-exericise control. However, there were no statistically significant main effects or interactions of CONGRUENCE, TIME, or EXERCISE (all $F < 1.48$, all $p > .243$, Figure 3.7).

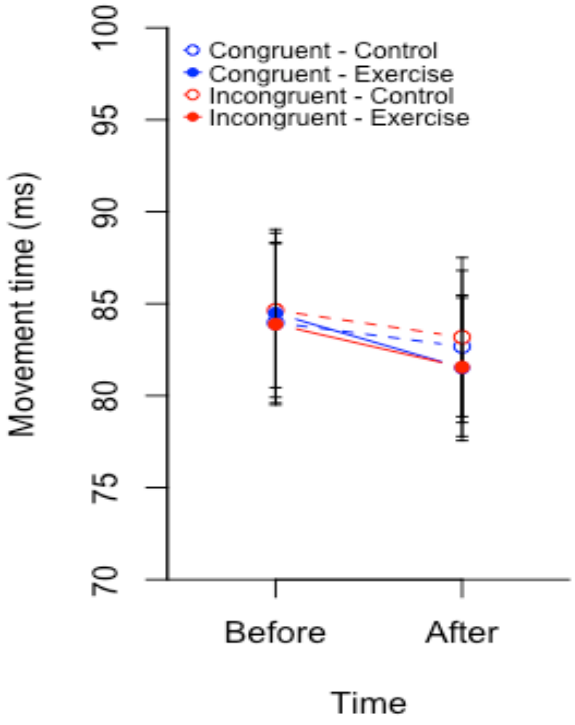

Figure 3.7. Movement time (mean ± SEM) on congruent and incongruent flanker trials before and after exercise and non-exercise control.

Response accuracy

Response accuracy (Figure 3.8A) was 8.2 % higher on congruent than incongruent flanker trials [97.3 (3.3) vs. 89.1 (8.5) %, $F_{(1, 15)} = 31.84$, $p < .001$, Figure 3.8B]. On incongruent flanker trials, response accuracy decreased 1.5 % from before to after intervention (i.e., exercise and control sessions collapsed) but decreased only 0.4 % on congruent flanker trials; however, neither the combined decrease over time ($F_{(1, 15)} = 4.17$, $p = .059$) nor the difference in decrease over time ($F_{(1, 15)} = 3.76$, $p = .072$) reached statistical significance. Response accuracy was not influenced by EXERCISE ($F_{(1, 15)} = 0.01$, $p = .928$).

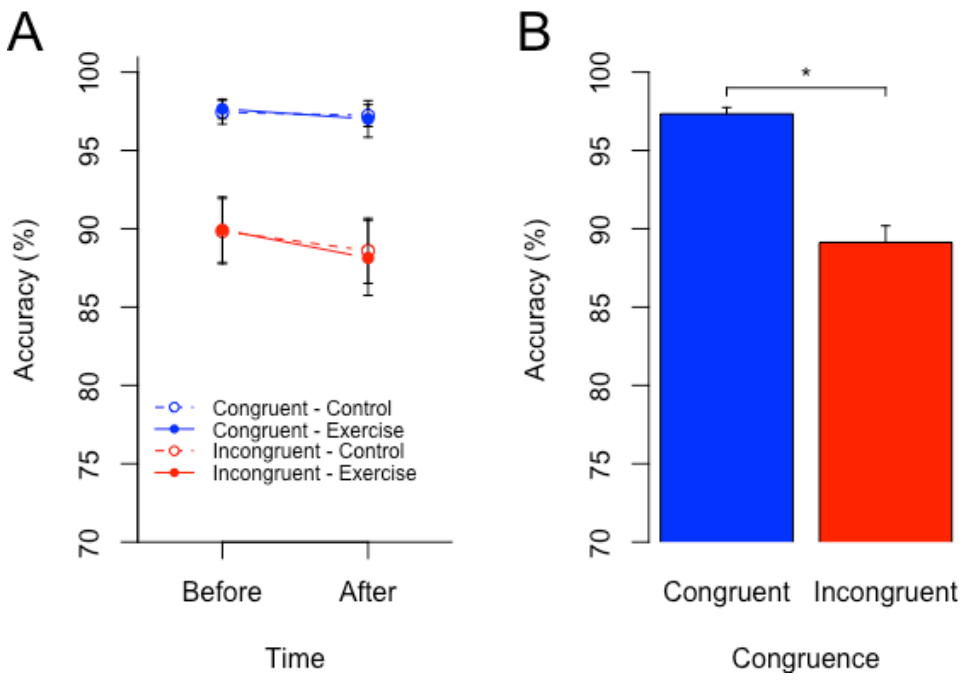

Figure 3.8. Response accuracy (mean ± SEM) on congruent and incongruent flanker trials before and after exercise and non-exercise control (A). Response accuracy on incongruent trials was significantly lower than on congruent trials (* $p < .001$, B).

3.4 Discussion

The present results do not support the hypothesis that a single session of aerobic exercise influences inhibitory control to reduce conflict during a flanker task. Contrary to our primary hypothesis, we did not observe a reduction in ERN amplitude, a measure of conflict-related cortical activity, immediately after aerobic exercise. Notably, this study did replicate previously reported behavioural and electrophysiological indications of conflict caused by incongruent flankers, but, contrary to previous reports, a single aerobic exercise session did not influence any behavioural or electrophysiological measure regardless of flanker congruency.

The current study demonstrated the well-known influence of flanker congruence on behaviour and electrophysiology; however, in contrast to some previous studies, a single session of aerobic exercise did not influence behaviour or electrophysiology regardless of flanker congruence. In the current study, response accuracy was lower, reaction time was longer, P3

amplitude was lower, and P3 latency was longer in incongruent flanker trials relative to congruent trials, as shown previously[64,65,75,97,100–102]. However, previous studies have also shown exercise-induced modulation of accuracy, response time, and P3 amplitude and latency, which were not observed in the present study[64,65,100–102]. Given this lack of exercise-induced change in other behavioural and electrophysiological markers of flanker-induced conflict it is not surprising that the present study failed to demonstrate an effect of exercise on ERN amplitude as a measure of conflict-related cortical activity. However, this result does support the previous finding that a single session of aerobic exercise does not influence ERN amplitude. One previous study found that, in young healthy adults, ERN amplitude measured during a flanker task performed after 30 minutes of vigorous aerobic exercise (i.e., mean HR was 82% of HR_{peak}) was not significantly different than after 30 minutes of quiet rest[135]. In this previous study, the ERN was measured a mean (sd) of 40.1 (13.9) minutes after exercise when HR had returned to within 10% of pre-exercise HR and compared to the ERN measured an unspecified amount of time after the control condition. Conversely, the present study measured the ERN immediately after the exercise session because that is when the greatest cognitive benefits occur[121]. As a result, the timing of the ERN measurement relative to the exercise or control task was also the same across all participants and sessions. However, similar to the previous study, the current study found that a single session of aerobic exercise did not significantly influence ERN amplitude. Taken together these findings suggest that a single session of aerobic exercise does not influence conflict as reflected by brain activity related to conflict monitoring. As such, the selective benefit of a single session of aerobic exercise on behavioural and electrophysiological markers of performance during incongruent flanker trials may not proceed from a reduction in conflict due to improved inhibitory control.

The lack of change in the ERN in response to exercise, however, may reflect a distinction between ACC activity related to error commission and conflict. The ERN is thought to reflect ACC conflict-related activity in response to errors and it is revealed by examining the response-locked frontocentral ERP of error trials only[83,86,103,104,188,189]. Conversely, exercise-induced behavioural and electrophysiological changes that are purported to indicate a reduction in conflict typically occur during correct trials. Selectively greater reduction in response time and P3 latency in incongruent trials, compared to congruent or neutral trials, after a single session of aerobic exercise is always shown by discarding error trials and analyzing these variables in correct trials only[64,65,100,101]. While not obvious using traditional ERP analysis, EEG analysis using current source density (CSD) or independent component analysis (ICA) has revealed a response-locked negativity similar to the ERN on correct trials, which has been called the correct-related negativity (CRN)[90,94,194,195]. Importantly, previous studies have shown that the CRN is sensitive to conflict when it is manipulated by flanker congruence[193,195]. Therefore, examination of conflict monitoring processes during correct trials may better reveal indications of this purported exercise-induced reduction in conflict.

While previous studies have shown exercise-induced changes in behaviour and electrophysiology during the flanker task, comparisons between exercise studies are not always consistent. For example, two previous studies indicate that response time is faster after a single session of exercise[101,102], two others indicate no effect of exercise[100,135], and two more indicate a reduced interference effect on response time after exercise[64,65]. Similarly, only one previous study shows a shorter P3 latency following exercise[102], two studies show no effect[64,65], and two show a reduced flanker interference effect[100,101]. Interestingly, only one of these studies showed both a shorter response time and P3 latency after exercise[102] while the other studies showed a

different influence of exercise for the two measures. Conversely, all of the previously mentioned studies have shown an increase in P3 amplitude after a single session of exercise while none have shown an influence on response accuracy[64,65,100–102,135]. The present study did not reveal an effect of exercise on any of these behavioural or electrophysiological measures regardless of flanker congruence and also showed no effect of exercise on ERN amplitude. Similarly, the previous study that did not show an influence of a single session of aerobic exercise on ERN amplitude also did not show any other exercise-induced behavioural or electrophysiological changes[135].

It is possible that methodological differences between studies may account for the disparity in exercise effects that have been detected in the literature. Narrative reviews[63,119] and meta-analyses[120,121] have indicated a number of participant and exercise parameters that moderate the influence of a single session of aerobic exercise on cognitive function, but differences in these parameters between this study and the previously mentioned studies are not obvious. There are, however, differences in the control time points to which post-exercise measures are compared. For example, some previous studies observe a shorter response time after exercise compared to a baseline measure on a separate day without any equivalent non-exercise control intervention[100–102,135]. Comparison of post-exercise response time – by adding reaction time and movement time – to the pre-control measure in the current study would yield a similar exercise-induced decrease in reaction time. This comparison would be inappropriate in the current study, but, as an example, it illustrates the importance of including the appropriate controls when examining the influence of exercise on cognition.

3.5 Conclusions

A single session of aerobic exercise did not reduce conflict as measured by the flanker interference effect on various behavioural and electrophysiological measures or by an EEG measure of conflict-related cortical activity (i.e., ERN amplitude). Exercise also did not influence any behavioural or electrophysiological measure regardless of flanker congruency, so, while not immediately apparent, examination of methodological differences between this study and previous studies may help explain the disparity in their findings. Recent evidence also suggests that error commission and conflict caused by incongruent flankers may have a separable influence on ACC activity, so study 3 examined the influence of a single session of aerobic exercise on conflict-related ACC activity separate from activity related to error commission.

Chapter 4: Study 3

Conflict-specific brain activity after a single aerobic exercise session

4.1 Introduction

Behavioural and electrophysiological changes following a single session of aerobic exercise suggest that exercise helps increase cognitive control to reduce conflict during information processing and improve task performance[64,135]. However, attempts to examine exercise-induced changes in conflict-related brain activity during error commission have not revealed changes that would reflect this reduction in conflict[135] (also see Chapter 3). Recent research suggests that conflict and error commission represent distinct events with separable effects on conflict-related brain activity[91] and potentially distinct responses to aerobic exercise. Conflict-related brain activity in the absence of errors is not usually apparent using traditional event-relate potential (ERP) analysis, so this study used novel electroencephalography (EEG) processing techniques, including independent component analysis (ICA), to isolate conflict-related brain activity from error-related brain activity and examine how this conflict-related activity is influenced by a single session of aerobic exercise.

While not evident in the previous studies of this dissertation, other work has suggested a single session of aerobic exercise has been shown to influence performance and electrophysiology during flanker task trials that require cognitive control to manage conflict. After exercise, there is a selectively greater reduction in response time and P3 latency in high-conflict incongruent flanker trials, compared to low- or no-conflict congruent or neutral

trials[64,65,100,101]. This reduction in flanker interference suggests greater use of cognitive control to reduce conflict. As a result, it has been suggested that a reduction in electrophysiological markers of conflict may be expected following exercise[135]. The error-related negativity (ERN) is a response-locked ERP component that reflects anterior cingulate cortex(ACC) conflict monitoring activity in response to errors caused by high levels of conflict[83,86,103,104,188,189]. Therefore, an exercise-induced reduction in ERN amplitude has been predicted but not supported empirically[135] (also see Chapter 3).

The lack of an exercise-induced influence on the ERN may be attributed to the separable influence of conflict and error on ACC conflict-monitoring activity[91]. Conflict is created when incongruent flankers activate inappropriate response pathways; behavioural errors are more likely to occur under high-conflict conditions[75,97]. It was previously suggested that error-related ACC activity reflects this high conflict level rather than the error itself [83,86]; however, a recent study suggests that conflict caused by incongruent flankers and error commission may represent distinct events monitored by the ACC[91]. As such, it is important to distinguish between these two types of events when examining the impact of aerobic exercise on conflict monitoring and cognitive control. Previous behavioural and electrophysiological indicators of an exercise-induced reduction in conflict have been extracted from high- and low-conflict trials during which the correct response was made, that is after error trials have been discarded[64,65,100,101]. A similar approach that examines ACC conflict-monitoring activity when an error is not present may provide additional information about how conflict is influenced by a single session of aerobic exercise.

While the ERN is revealed by examining the response-locked frontocentral ERP of error trials only[103,104], a response-locked negativity, similar to the classic ERN but smaller in

amplitude, also occurs on correct trials and has been called the correct-related negativity[90,91,194,195] (CRN). The CRN is not usually obvious using traditional ERP analysis that employs cross-trial averaging of monopolar EEG data to reduce the signal-to-noise ratio but can be revealed by current source density (CSD) or ICA transformations[90,94,194,195]. ICA can be applied to EEG data to parse the aggregate signal into independent source components, each with its own time-varying activity and a constant scalp topography[196–198]. Based on these characteristics, an independent component or components can be identified that account for specific ERP features of interest. As such, the CRN may be revealed by identifying a single independent component characterized by a frontocentral topography and a time course that features a peak negativity immediately following the onset of a correct response[90,195]. Source localization and time-frequency analysis indicate that, like the ERN, the CRN is generated by modulation of theta-band phase and power dynamics from a source within the rostral cingulate zone[91,195]. However, compared to the ERN, the CRN has a shorter latency and a smaller amplitude[193,195]. Importantly, the CRN also appears to be influenced by induced conflict: during the flanker task, CRN amplitude is larger on incongruent than congruent trials[193,195]. Therefore, because the CRN reflects conflict-related ACC activity separate from confounding error-related activity, it may be used to reveal additional information about the influence of aerobic exercise on conflict.

The primary purpose of this study was to examine the influence of a single session of aerobic exercise on conflict-related brain activity during a flanker task. ICA was used to reveal the response-locked CRN as a measure of conflict-related brain activity. Exercise is thought to reduce flanker interference by increasing cognitive control to reduce conflict. Therefore, the primary hypothesis was that there would be a reduction in CRN amplitude following exercise,

particularly during incongruent flanker trials, indicating a reduction in conflict caused by incongruent flanker stimuli. A secondary objective was to examine how the conflict-related brain activity captured by the CRN was influenced by induced conflict and error commission. Because incongruent flanker trials are meant to induce greater conflict, it was hypothesized that CRN amplitude during incongruent flanker trials would be greater than during congruent trials reflecting greater conflict-related brain activity. Furthermore, since the CRN and ERN have been shown to share a common neural source, it was predicted that the same independent component would reveal the ERN on error trials. It was hypothesized that the ERN would be distinguishable from the CRN by its larger amplitude and longer latency. Revealing how a single session of aerobic exercise influences conflict-related brain activity independent of error-related activity generated by a common neural source will link previously observed behavioural changes following exercise to underlying brain activity. This link represents an important step toward understanding how aerobic exercise influences cognitive control and overall cognitive function.

4.2 Methods

This study used data previously collected as described in study 2 (see Chapter 3) but relevant methodology is included here for convenience. The EEG data processing and statistical analysis described below are unique to this study.

Participants

Sixteen healthy, young adults (8 female) volunteered to participate in this study. This study was approved by the Office of Research Ethics at the University of Waterloo and all participants provided written informed consent before participating. Participants were screened

for exclusion criteria including musculoskeletal or neurologic disorders that may have affected their ability to perform the study and their readiness to exercise without requiring permission from their physician (Physical Activity Readiness Questionnaire, Canadian Society for Exercise Physiology, Ottawa, ON).

Experimental protocol

Each participant volunteered to visit the laboratory for three separate sessions: 1) screening and graded exercise test, 2) exercise session, and 3) non-exercise control session. The first session preceded the second session by 2-17 days; the second and third session were 2-7 days apart. All three sessions were performed at the same time of day for each participant. The order of the last two sessions and time-of-day of both sessions were counter-balanced across participants.

Upon arrival for the first session, participants were provided information about the study before consenting to participate. During this initial session, participants received instruction and familiarization with the Borg Rating of Perceived Exertion (RPE) and the magnetic-resistance recumbent cycle ergometer that was used throughout the experiment. Participants then performed the graded exercise test (GXT) to establish aerobic fitness levels and determine the work rate for the exercise session.

Participants started both experimental sessions (exercise and non-exercise) seated in a chair in front of a computer monitor. After sitting quietly for two minutes while resting heart rate was measured, participants performed four 100-trial blocks of the flanker task for practice. After a four-minute break, participants then performed five more blocks of the flanker task before being seated on the cycle ergometer. In the exercise session, participants were then allowed five

minutes to warm up before exercising for 30 minutes. In the non-exercise control session, participants sat quietly on the recumbent cycle ergometer for 35 minutes without pedalling. Immediately after exercise or non-exercise control participants returned to the chair in front of the computer monitor to perform five more blocks of the flanker task.

Graded exercise test

Each participant performed a GXT on the cycle ergometer to measure peak oxygen consumption (VO_2peak) and determine the work rate for the experimental exercise session. Before starting the test, participants rested quietly for 2 minutes. The test started with the participant pedaling at a rate greater than 55 revolutions per minute (RPM) at effort level 3. Every two minutes the effort level was increased by 4 until the participant chose to stop or could no longer maintain a pedal rate of 55 RPM. Effort levels on the cycle ergometer were chosen to start at a power of 50 W while pedaling at 55 RPM and increase 50 W every two minutes if the same pedal rate is maintained.

Throughout the test, respiratory gases were analyzed breath-by-breath (Vmax 229, SensorMedics Inc., Palms Springs, CA) and electrocardiogram (ECG) was measured continuously. Gas analysis and ECG were transmitted to computer software (Vmax Vision, SensorMedics Inc., Palms Springs, CA) for calculation of variables of interest [e.g., oxygen consumption (VO_2), respiratory exchange ratio (RER), and heart rate (HR)]. These variables were displayed in real-time and stored for offline processing and analysis. RPE was measured at the beginning of each work level. Offline, VO_2, RER, and HR were averaged over 20-second intervals. Resting VO_2 was the mean VO_2 during the 2-minute rest period prior to exercise. VO_{2peak}, RER_{peak}, RPE_{peak}, and HR_{peak} were calculated as the respective peaks achieved during

the GXT. Oxygen uptake reserve (VO_2R) was calculated as the difference between VO_{2peak} and resting VO_2.

GXT results were compared to commonly used pre-determined criteria [169] to test whether each participant achieved a true VO_{2peak}. The primary criterion was an increase in VO_2 of less than or equal to 2.1 ml/kg/min after an increase in workload. Secondary criteria were a RER_{peak} greater than 1.1, RPE_{peak} greater than 9, HR_{peak} greater than 90% of age-predicted (i.e., 220 – age). To be deemed a true VO_{2peak} the primary criterion or at least two of the secondary criteria must have been achieved during the test.

Exercise and associated measures

During the experimental exercise session, each participant performed a 30-minute session of exercise on a magnetic-resistance recumbent cycle ergometer (Excite 700iP, Technogym, Fairfield, NJ). Exercise intensity was set and monitored using the work level, RPE, and HR coinciding with 40-59% VO_2R during the participant's GXT. Throughout the warm-up and exercise participants pedalled at a self-selected comfortable rate while the work level was adjusted by the researcher to maintain the desired intensity. Each participant began the 5-minute warm-up pedaling at work level 3 while the researcher gradually increased the work level to that coinciding with 40% VO_2R. During the 30-minute exercise session participants continued to pedal at a self-selected comfortable rate while the researcher adjusted the work level to maintain a HR in the range coinciding with 40-59% VO_2R. A switch on the cycle ergometer indicated each revolution of the pedals and was used to calculate pedal rate.

Electrocardiography. For the GXT, exercise, and non-exercise control sessions ECG was collected continuously (EK-10, Burdick Inc., Milton, WI). Electrodes were placed at the center

of the manubrium and bilaterally over the 5th intercostal space along the mid-clavicular line. Data were sampled at 1,000 Hz and stored for offline processing. ECG was used to calculate heart rate (HR) in beats per minute (BPM). During exercise, a real-time heart rate was calculated and displayed to monitor exercise intensity.

Borg Rating of Perceived Exertion. RPE[170] was used to monitor exercise intensity. Throughout the graded exercise test and exercise session, the participant was asked to verbally rate their perceived exertion on a scale from 0 (nothing at all) to 10 (very, very strong).

Flanker task and associated measures

Before and after exercise or non-exercise control, participants sat in a chair in front of a computer monitor to perform a modified Eriksen flanker task[75,102] delivered via custom software (LabVIEW, National Instruments, Austin, TX). Participants fixated on a point in the center of the screen while stimuli were presented. They began each trial with their hands supported prone on a table in front of them, each thumb resting on a button. In each trial a target stimulus was presented consisting of a right or left pointing arrow (i.e., > or <). The target stimulus was flanked by 4 additional arrows, two on each side, that were either congruent (< < < < < or > > > > >) or incongruent (< < > < < or > > < > >) with the target arrow. Participants responded by pressing a button with their right or left thumb as quickly as possible as indicated by the target arrow. A stimulus was presented for 100ms every 2 seconds and participants were allowed 1500ms to respond. In each block, 25 stimuli of each condition were presented in random order for a total of 100 trials. A voltage output indicating whether the button was pressed or not was sampled at 1,000 Hz and stored for offline processing.

Electromyography. Reaction time was determined from the onset of muscle activity preceding a button press with the thumb. Bilateral flexor pollicis brevis electromyography (EMG) was measured to determine the onset of muscle activity. Electrodes were placed on the muscle belly bilaterally and another electrode was placed on the left ulnar styloid process to act as a ground. Data were amplified (x 500), filtered (10 to 1,000 Hz) (AMT-8, Bortec Biomedical, Calgary, AB), sampled (1,000 Hz), and stored for offline processing.

Electroencephalography. To record brain activity, EEG was recorded from 30 channels using Ag/AgCl electrodes arranged according to the International 10-20 system[190] and embedded into a Lycra cap (Quik-Cap, Compumedics Neuroscan, Charlotte, NC). To record eye movements and blinks, electrooculography (EOG) was recorded using Ag/AgCl electrodes placed above and below the left eye and lateral to the outer canthus of both eyes. For both EEG and EOG, an electrode at AFz was used as a ground and all electrodes were referenced to the average activity of electrodes located over the left and right mastoid. Impedances for all electrodes were below 5 kΩ. For each block of flanker trials, continuous EEG was amplified (x 19), filtered (DC to 300 Hz), and sampled (1000 Hz) using a Neuroscan amplifier (NuAmps, Compumedics Neuroscan, Charlotte, NC) and software (Scan, Compumedics Neuroscan, Charlotte, NC).

Data processing

EMG signals were bandpass filtered (20-500 Hz), baseline corrected, and full-wave rectified (FWR EMG) before being low-pass filtered (50 Hz; smoothed EMG). FWR and smoothed EMG were used to determine flexor pollicis brevis muscle activity onset using the following criteria: 1) FWR and smoothed EMG must both exceed a threshold equal to the mean

plus 3 standard deviations of a 100-ms pre-stimulus baseline and 2) smoothed EMG must remain above this threshold for at least 25 ms.

Each trial was assigned a response status based on the muscle activity and button press response to the stimulus as follows: 'no response' when neither button was pressed, 'correct response' when only the correct button was pressed, 'incorrect response' when only the incorrect button was pressed, 'remedial response' when the incorrect button was pressed followed by the correct button, 'partial incorrect response' when muscle activity on the incorrect side preceded a correct button press, and 'undefined' for any other combination of button presses.

EEG data was band-pass filtered (1 to 100 Hz). Epochs were extracted around the onset of each flanker stimulus (-1000 to 1750 ms) and baseline corrected (-500 to -400 ms). Each epoch was visually inspected and rejected if electrodes contained large amplitude voltage changes indicating noise other than eye artifact. ICA was then performed using the extended Infomax algorithm[191]. Independent components were visually inspected and those representing eye and muscle artifact were removed. Each epoch was visually inspected again for additional noise removal. Electrode voltages were compared to independent component activations to determine if remaining noise could be removed by epoch rejection or independent component rejection.

To examine the CRN, epochs were created around the appropriate EMG response for correct trials (-1000 to 1000 ms), baseline corrected (-1000 to -800 ms), and band-pass filtered (0.1 to 50 Hz). ICA was performed again on these response-locked epochs. For each participant, a single IC was selected that best resembles the scalp topography and time-course of the CRN. To aid in IC selection, an algorithm was created to rank all ICs based on their activity 50 to 250 ms following EMG onset in correct trials. This algorithm accounted for 1) the amplitude of the

negative peak in the component ERP, 2) the correlation of individual trial component activity and FCZ electrode voltage, and 3) the correlation of the component ERP to the FCZ ERP during this time window. From the top 5 ranked ICs, a single IC was selected that had a fronto-central radial topography and a clear negativity following response onset in correct trials [90,195]. This IC was then back-projected to the scalp and examined at the FCz electrode. All EEG data was then band-pass filtered (0.5 to 15 Hz) and averaged across the appropriate trials to obtain ERPs that contained the CRN on congruent and incongruent correct trials and the ERN on incongruent error trials. For each ERP, the negative peak (i.e., trough) voltage at the FCz electrode between 50 and 250 ms after EMG onset was identified along with the positive peaks immediately preceding and following. CRN and ERN amplitudes were calculated by subtracting the mean of the two positive peaks from the negative peak. CRN or ERN latency was the time from EMG onset to the negative peak voltage. ERN, and CRN when compared to ERN, was examined in 10 participants that made at least five remedial responses[192,193] in each block (i.e., before and after both interventions). Only remedial trials were used as error trials as we wanted to be sure that participants knew they had committed an error.

Statistical analysis

To pursue the primary objective of this study, we examined the influence of flanker congruence, exercise, and time on mean CRN amplitude using a repeated-measures analysis of variance (ANOVA) with three factors: CONGRUENCE (2 levels: congruent and incongruent), EXERCISE (2 levels: exercise and non-exercise control), and TIME (2 levels: before or after exercise or control). The influence of flanker congruence, exercise, and time on CRN latency were also examined using an identical repeated-measures ANOVA. Differences in amplitude and

latency between CRN and ERN, along with the potential influence of exercise and time, were examined using separate repeated-measures ANOVAs with ACCURACY (2 levels: correct and error), EXERCISE (2 levels: exercise and non-exercise control), and TIME (2 levels: before or after exercise or control). An alpha level of $p <= .05$ was used to denote statistical significance.

4.3 Results

CRN

Grand-average (N = 16) response-locked ERPs showing the CRN at FCz electrode site are presented in Figure 4.1. Mean (sd) CRN amplitude (Figure 4.2A) was 0.40 μV larger during the exercise session than the non-exercise control session [-1.81 (1.20) vs. -1.41 (0.93) μV, $F_{(1, 15)} = 5.62$, $p = .032$, Figure 4.2B]. CRN amplitude decreased 0.31 μV from before to after exercise but also decreased 0.11 μV from before to after control; however, neither of these decreases were statistically significant as there were no statistically significant main effects or interactions involving TIME (all $F < 2.72$, all $p > .117$). CRN amplitude was not significantly influenced by CONGRUENCE ($F_{(1, 15)} = 1.68$, $p = .215$).

CRN latency, averaged across all sessions, task conditions, and time points, was 111.1 (60.7) ms. CRN latency, collapsed across congruence, increased 25.2 ms from before to after exercise, but decreased 2.4 ms shorter from before to after non-exercise control. However the interaction between EXERCISE and TIME was not statistically significant ($F_{(1, 15)} = 1.72$, $p = .209$, Figure 4.3). There were also no statistically significant main effects of EXERCISE, TIME, or CONGRUENCE (all $F < 3.05$, all $p > .101$).

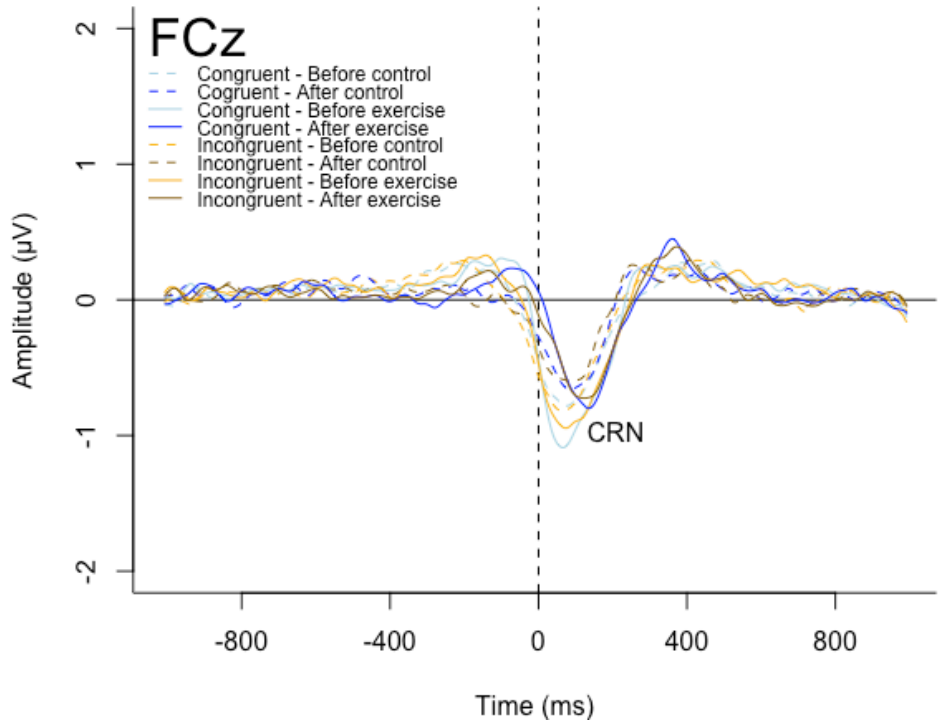

Figure 4.1. Response-locked (i.e., EMG onset) ERP showing the CRN on congruent and incongruent flanker trials before and after exercise and non-exercise control. ERP is the grand average at FCz electrode site of all participants (N = 16). EMG onset is denoted by the vertical dashed line at time 0.

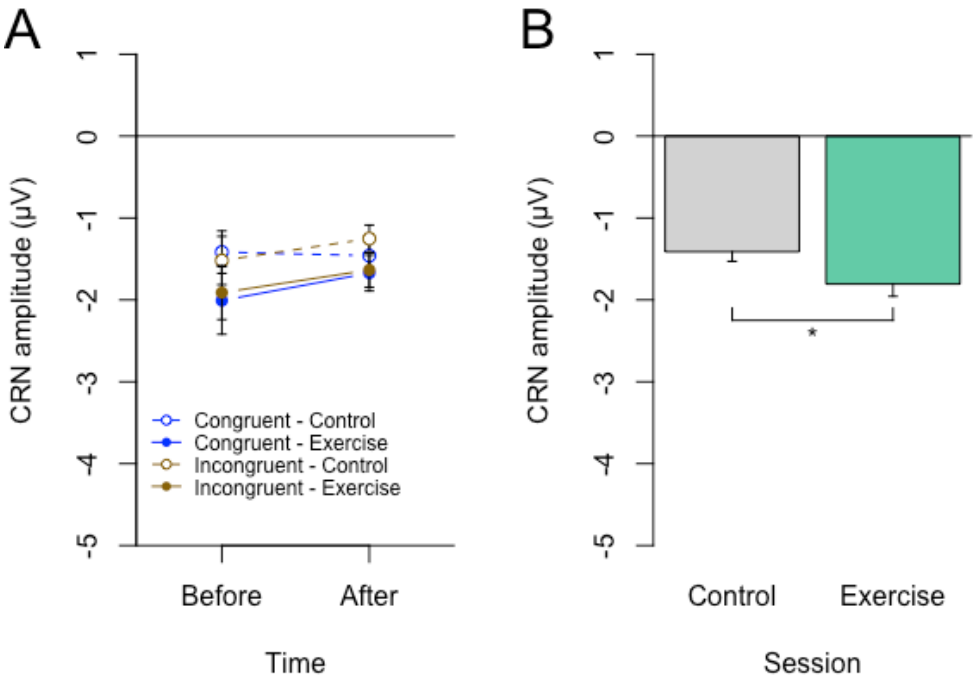

Figure 4.2. CRN amplitude (mean ± SEM) on congruent and incongruent flanker trials before and after exercise and non-exercise control (A). CRN amplitude during the exercise session was significantly larger than during the control session (* p = .032, B).

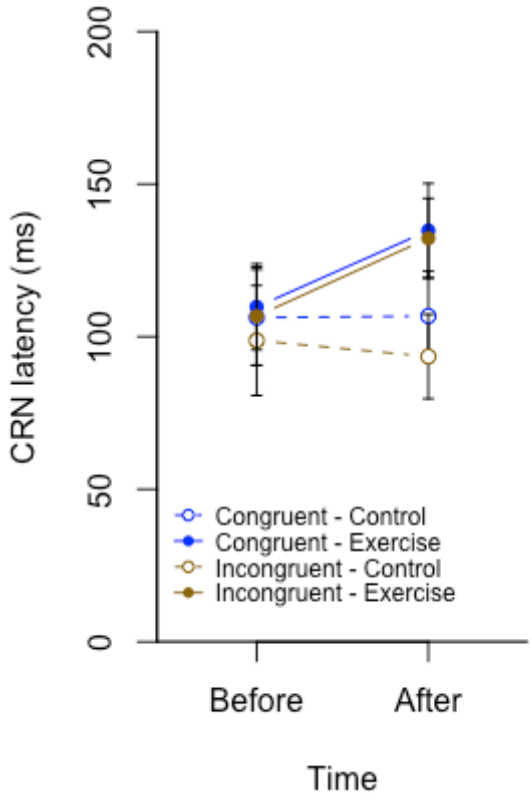

Figure 4.3. CRN latency (mean ± SEM) on congruent and incongruent flanker trials before and after exercise and non-exercise control.

CRN vs. ERN

Using the same independent component selected to reveal the CRN, analysis of incongruent error trials revealed an ERN with a mean peak amplitude of -2.61 (2.96) μV and latency of 169.6 (54.0) ms (Figure 4.4). CRN amplitude (Figure 4.5A) during incongruent correct trials was 1.09 μV smaller than mean ERN amplitude, but this difference did not reach statistical significance [-1.52 (1.14) vs. -2.61 (2.96) μV, $F_{(1, 9)} = 4.39$, $p = .066$, Figure 4.5B]. ERN amplitude appeared to decrease more over time than CRN amplitude but the interaction between ACCURACY and TIME was not statistically significant ($F_{(1, 9)} = 2.45$, $p = .152$). There were no significant main effects or interactions involving EXERCISE (all $F < 0.59$, all $p > .461$).

CRN latency (Figure 4.6A) was 64.9 ms shorter than ERN latency [104.7 (61.0) vs. 169.6 (54.0) ms, $F_{(1, 9)} = 31.70$, $p < .001$, Figure 4.6B]. When collapsed across both time points in the exercise session, CRN latency was 26.2 ms longer and ERN latency was 4.4 ms shorter than the control session, but the interaction between EXERCISE and ACCURACY did not reach statistical significance ($F_{(1, 9)} = 3.41$, $p = .098$). Both CRN and ERN latency appeared to increase during the exercise session but decrease during the control session; however, the interaction between EXERCISE and TIME also was not statistically significant ($F_{(1, 9)} = 1.92$, $p = .201$). No other main effects or interactions were statistically significant (all $F < 0.78$, all $p > .401$).

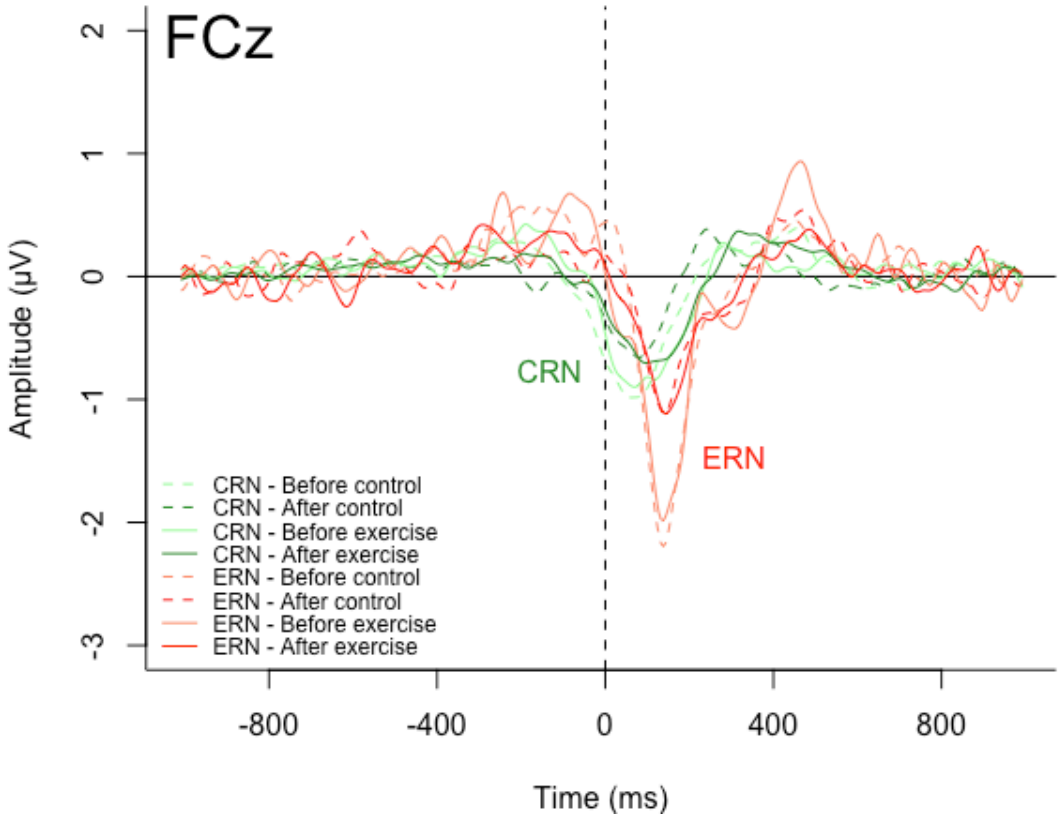

Figure 4.4. Response-locked (i.e., EMG onset) ERP showing the CRN and ERN on incongruent flanker trials before and after exercise and non-exercise control. ERP is the grand average at FCz electrode site of all participants with at least 5 remedial trials in all conditions (N = 10). EMG onset is denoted by the vertical dashed line at time 0.

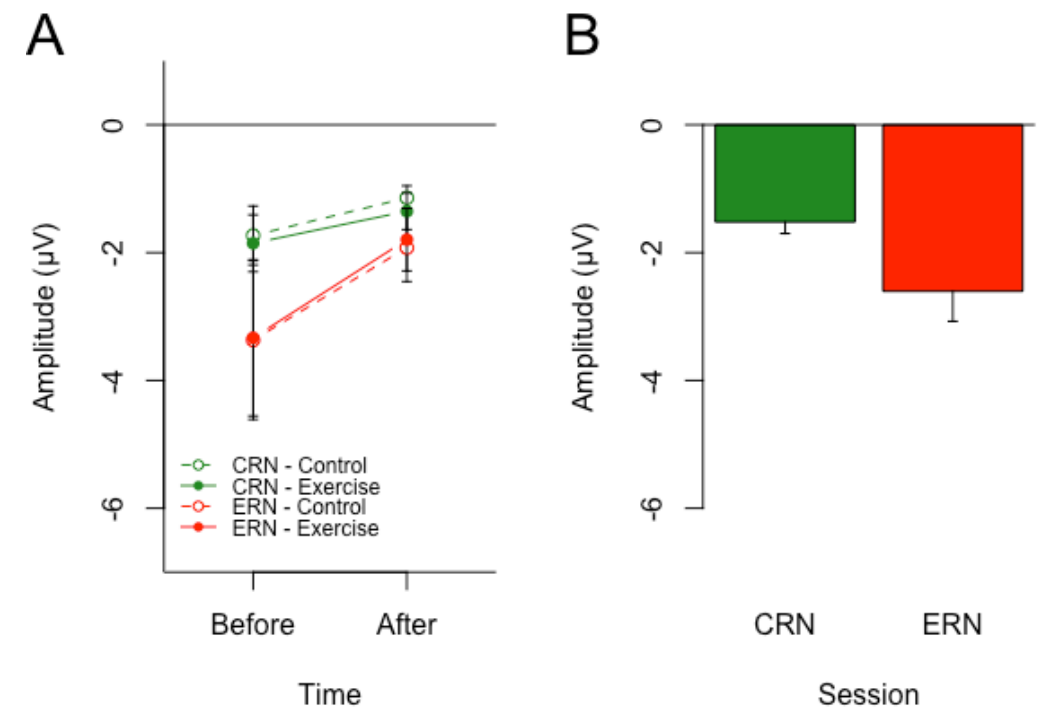

Figure 4.5. CRN and ERN amplitude (mean ± SEM) on incongruent flanker trials before and after exercise and non-exercise control (A). CRN amplitude was smaller than ERN amplitude, but this difference did not reach statistical significance (p = .066, B).

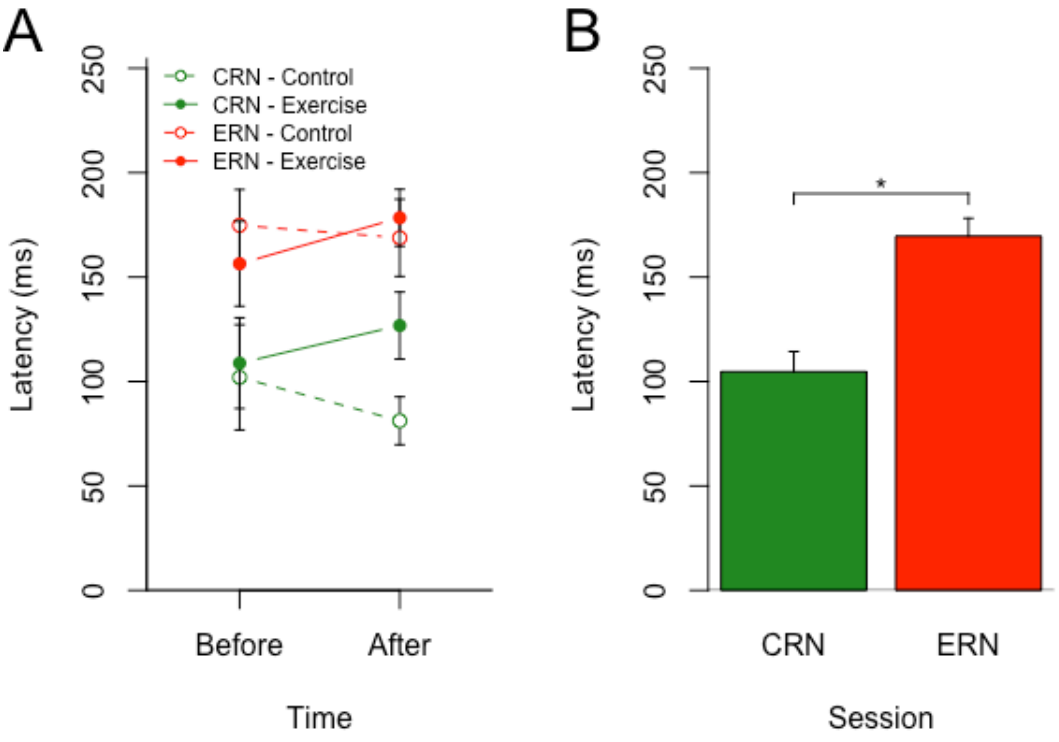

Figure 4.6. CRN and ERN latency (mean ± SEM) on incongruent flanker trials before and after exercise and non-exercise control (A). CRN latency was significantly shorter than ERN latency (* p < .001, B).

4.4 Discussion

This study examined how a single session of aerobic exercise influenced conflict-related brain activity during a flanker task. Because previous behavioural and electrophysiological studies suggest a reduction in conflict following aerobic exercise, we hypothesized that conflict-related brain activity, as measured by CRN amplitude, would also be reduced; however, the present results do not support this hypothesis. CRN amplitude after exercise was not lower than before exercise; rather, when collapsed across all other factors, CRN amplitude was higher during the exercise session than the non-exercise control session. Furthermore, contrary to our hypothesis, CRN amplitude was not influenced by flanker congruence indicating that, as a trial-averaged ERP feature, the CRN may not reflect brain activity related to conflict caused by flanker interference. The present results do support our hypothesis that an independent component selected to reveal the CRN on correct trials would also reveal the ERN on error trials. Analysis of error trials revealed an ERN that had a larger amplitude and longer latency than the CRN; although, the amplitude difference did not reach statistical significance.

In the present study, a single session of aerobic exercise did not reduce conflict-related brain activity as measured by CRN amplitude during a flanker task. Previous studies indicate that CRN amplitude is modulated by flanker congruence suggesting its role in conflict monitoring[193]. In the present study, CRN amplitude on both congruent and incongruent flanker trials decreased slightly from before to after exercise but this decrease, particularly during incongruent trials, did not differ from the rest condition and was not statistically significant. In fact, CRN amplitude was significantly higher in the exercise condition compared to the rest condition (when collapsed across time points and flanker congruence) suggesting an exercise-induced increase in conflict-related brain activity. These results contradict previous studies showing a reduction in response

time and P3 latency on incongruent trials relative to congruent or neutral trials after exercise suggesting a reduction in conflict[64,65,100,101]. However, these results do coincide with previous electrophysiological work indicating that brain activity related to error commission, another source of conflict monitored by the ACC, also does not decrease following exercise. Themanson & Hillman[135] measured ERN amplitude after heart rate returned to baseline (mean ~40 minutes) following a 30-minute aerobic exercise session and found that it did not differ from resting control. Our previous work has confirmed that ERN amplitude also does not decrease immediately after exercise compared to before exercise or after a non-exercise control session (see Chapter 3). In the current study, we also measured ERN by looking at error-related activity of the independent component selected to reveal CRN. We again found no influence of exercise on ERN amplitude. The lack of a reduction in conflict-related brain activity after a single session of exercise in the current and previous studies does not support the suggestion that selectively greater behavioural and electrophysiological changes on high-conflict tasks indicates an exercise-induced reduction in conflict.

The disparity between studies showing an exercise-induced improvement in conflict-related behaviour and electrophysiology and others, like this one, showing no change in conflict-related brain activity suggest that aerobic exercise may influence cognitive processes that do not affect internally experienced conflict. For example, P3 latency decreases after aerobic exercise[100–102] may reflect a reduction in stimulus evaluation time[184]. The selectively greater effect on P3 latency during incongruent trials[100,101] may reflect the longer time taken to evaluate those more complex stimuli. A shorter stimulus evaluation time could also explain the shorter response time, particularly on incongruent trials, as seen in other studies[64,65]. Previous studies have also shown that exercise influences the excitability of neurons in the primary motor

cortex[173], specifically supressing inhibitory and facilitating excitatory intracortical networks[174–177]. It remains unclear how this change in motor cortical excitability influences performance on tasks that induce conflict. Further research is required to disentangle how aerobic exercise benefits conflict-related behaviour and electrophysiology without influencing conflict-related brain activity.

An alternative explanation for the disparity between the present lack of an exercise-induced reduction in brain activity and previous behavioural and electrophysiological studies suggesting a reduction in conflict is that the CRN, as measured here, does not adequately reflect brain activity related to conflict. The findings of the present study support previous literature indicating that the CRN is generated by a neural source known to be involved in conflict monitoring[91,195]. We found that the same independent component selected to reveal the CRN on correct trials also revealed the ERN on error trials. Coincident with previous literature, the ERN had a larger amplitude and longer latency than the CRN[193,195]. This evidence suggests that the CRN reflects conflict-related brain activity; however, contrary to previous literature this brain activity in the current study was not related to conflict induced by flanker incongruence[193,195]. Previously, using traditional cross-trial averaging to reveal the CRN, Bartholow et al.[193] reported a mean CRN amplitude across all conditions of -2.6 μV, whereas the present study, using ICA, found a mean CRN amplitude of -1.61 μV. Importantly, Bartholow et al.[193] also showed that CRN amplitude during incongruent flanker trials was 0.6 μV larger than during congruent flanker trials, a statistically significant difference. However, in the present study we found that CRN amplitude during incongruent trials was 0.06 μV smaller than during congruent trials, but this difference was not statistically significant. In comparing the results of these two studies it becomes obvious that methodological differences may explain the disparity between them.

A variety of EEG processing techniques have been used to extract the CRN signal from the raw EEG signal. Bartholow et al.[193] employed traditional cross-trial averaging without any additional transformations while the present study used ICA to identify a single independent component that represented the CRN. Two studies have used ICA in a similar manner to isolate the ERN and then examine the selected component in correct trials to reveal the CRN[90,195]. Roger et al.[195] examined the CRN using traditional cross-trial averaging as well as using CSD and ICA transformations noting the similarities between the CRN revealed by CSD and ICA; however, flanker congruence only influenced the CRN amplitude when revealed using CSD. Studies have also examined the CRN at different electrode sites. The present study examined the CRN at the FCz electrode based on previous research indicating the highest CRN amplitude at this site[194]. Bartholow et al.[193] collected EEG from 20 electrodes according to 10-20 placement that likely did not include an FCz electrode and found the highest CRN amplitudes at electrode Cz. CRN amplitude has also been quantified in different ways across studies. For example, Bartholow et al.[193] quantified CRN amplitude as the average voltage in the 10 to 110 ms window following response onset (i.e., a keypress) relative to the average of the 50 ms preceding response onset. In the current study, we quantified CRN amplitude as the peak negative voltage in the 50 to 250 ms window following EMG onset relative to the mean of the preceding and following peaks. All of the previous studies examining the CRN are limited by the traditional approach of averaging across trials to obtain an ERP. Namely, trial-to-trial variability in the latency of the CRN within a participant acts to flatten and diminish its amplitude possibly preventing the accurate measurement of conflict-related brain activity. Further research should evaluate different tools, such as ICA, that may allow a standardized single-trial measure of the CRN.

This study did not observe previously reported changes in behaviour and electrophysiology after exercise, limiting its ability to link exercise-induced changes in brain activity and behaviour. Reaction time and P3 data from this dataset has previously been reported (see Chapter 3). While previous studies have shown a reduction in response time and P3 latency and an increase in P3 amplitude following exercise[64,65,100–102,135], none of these changes were observed in the current dataset. A number of participant, exercise, and cognitive task characteristics have been revealed to moderate the relationship between a single session of exercise and subsequent cognitive function[63,119–121]. A better understanding of these moderators will help to understand how methodological difference between exercise studies may be contributing to the disparity in their observed influence on cognitive function.

4.5 Conclusions

In this study, a single session of aerobic exercise did not reduce conflict-related brain activity as measured by CRN amplitude suggesting that aerobic exercise does not benefit cognitive control processes that reduce conflict. However, CRN amplitude also was not influenced by varying levels of conflict challenging the purported role of the CRN in monitoring conflict. The limitations of the traditional approach of averaging across trials to obtain an ERP may have limited the accurate measurement of conflict-related brain activity in this study. As a result, study 4 advanced a novel use of ICA to permit the examination a single-trial measure of the CRN and its relationship to behaviour during the flanker task. This single-trial approach has the potential to provide new insight into brain-behaviour relationships during cognitive control tasks by exploiting the important influence of conflict on behaviour both within and between individual trials.

Chapter 5: Study 4

Single-trial evaluation of conflict-related brain activity

5.1 Introduction

In order to examine whether a single session of aerobic exercise impacts the ability of cognitive control to resolve conflict during choice reaction tasks, it is important to first understand the relationship between conflict-related brain activity and behaviour. Single trial analysis represents an important step in understanding the link between time-varying brain activity and behaviour related to monitoring and controlling conflict during information processing. Certain behavioural tasks are designed to promote conflict, the simultaneous activation of multiple response pathways, by presenting irrelevant distractor information that promotes a response that is incompatible with the correct response. Higher conflict leads to a predictable decline in behavioural performance but is also evaluated by conflict monitoring networks to adjust cognitive control and improve future performance. While the influence of conflict on behaviour and brain activity has been observed, the link between this brain activity and behaviour remains unclear. This study used a single-trial electroencephalography (EEG) measure to explore the dynamic relationship between trial-to-trial variability in brain activity and behavioural performance related to conflict.

An important facet of understanding cognitive function is linking brain activity to behaviour during cognitive tasks. It has become increasingly apparent that examining single trial data is crucial to understanding this relationship between brain activity and behaviour[82,199–203]. Single trials are considered the fundamental unit of behaviour in cognitive neuroscience;

however, while performing a cognitive task, both brain activity and behavioural performance vary from trial to trial[82,201,203]. For behavioural data, such as reaction time, it is largely unknown what causes this trial-to-trial variability when it cannot be controlled experimentally, so it has historically been treated as noise and averaged away leaving a representative estimate of the measure[201,203]. Similarly, averaging of brain activity is based on the assumption that the signal will persist when averaged across multiple trials, but the noise will be reduced to near zero, so the average should represent a single noiseless trial[82,199,200]. When averaging both behavioural performance and brain activity across trials, it is important to remember that we are left with an estimate that represents central tendency but may not represent a single individual trial[200]. Considering that behavioural performance in daily life (e.g., safety, success) is typically defined by the outcome of a single behaviour rather than the average of many, a better understanding of this relationship between trial-varying brain activity and behaviour may be essential to understanding control of behaviour and cognitive function.

The relationship between trial-varying brain activity and behaviour related to conflict has not yet been explored. Conflict occurs when the presentation of irrelevant distractor information during a choice reaction task leads to the activation of multiple response pathways and predictably diminishes mean behavioural performance[74]. Cognitive tasks such as the Stroop[72], Simon[73,74], and flanker task[75] create conflict by presenting distractor information that may be neutral, reinforce the correct response (i.e., congruent trials), or promote the incorrect response (i.e., incongruent trials). During the flanker task, a participant is asked to respond to a central target stimulus while distractor information is presented via irrelevant stimuli on either side of the central target[75] (i.e., flankers). Reaction time and accuracy depend on flanker congruency: participants respond faster and commit fewer errors during congruent trials compared to

incongruent trials[75,83,86,87,97]. Induced conflict is often categorized by the stimulus category (e.g., neutral, congruent, or incongruent) while internally experienced conflict is often quantified by calculating the flanker interference effect, the difference in mean reaction time or response accuracy between neutral or congruent and incongruent trials[82].

Conflict is also thought to be evaluated by the conflict monitoring network, so measurement of brain activity generated by this network may also be used to quantify internally experienced conflict. The conflict monitoring network consists of structures in the medial prefrontal cortex (mPFC), including the anterior cingulate cortex (ACC), that evaluate conflict during information processing that may arise from many sources such as conflict or error commission[204]. EEG and fMRI studies show that the ACC responds to both the commission of an error and to high levels of conflict supporting its putative role in conflict monitoring[82,86–92]. Therefore, if ACC activity is modulated by internally-experienced conflict that, in turn, causes diminished behavioural performance, there should be a relationship between variability in this conflict-related brain activity and behaviour.

While manipulation of the conflict induced by a stimulus may be discrete (i.e., high conflict vs. low or no conflict), internally experienced conflict varies from trial to trial even within the same conflict category[82]. Single-trial analysis has revealed that trial-to-trial variability in brain activity related to error commission is linked to trial-to-trial variability in behaviour but the link between variability in brain activity related to conflict and behaviour is less clear. The error-related negativity (ERN) is a measure of conflict-related brain activity revealed by examining the response-locked fronto-central event-related potential (ERP) after the commission of an error[103,104]. Single-trial analysis has shown that higher ERN amplitude is associated with shorter reaction time indicating a relationship between brain activity caused by error commission

and behavioural performance during the commission of the error[90]. The correct-related negativity (CRN) is an ERP feature with similar spatial and temporal characteristics as the ERN but is observed following a correct response[91,194,195]. Importantly, the CRN appears to be influenced by conflict – CRN amplitude measured from trial-averaged ERP is larger on incongruent flanker trials than congruent trials[193,195] – suggesting its role in conflict monitoring. However, unlike with the ERN, the relationship between the CRN and behaviour has not been explored. A similar analysis – employing a single-trial measure of the CRN to characterize the relationship between trial-to-trial variability in brain activity and behaviour that are both influenced by conflict – is an important step towards understanding cognitive function related to the evaluation and control of conflict.

Single trials may be the fundamental unit of behaviour, but performance is dependent on prior trials and experience, so characteristics of a given trial (e.g., conflict, performance) likely influence subsequent trials. Conflict monitoring and cognitive control networks work together to dynamically optimize performance during goal-directed behaviour[82,83,87,93,94,204]. The cognitive control network consists of structures in the lateral prefrontal cortex (lPFC) that exert a top-down influence on other brain structures to reduce conflict and optimize information processing. As the conflict monitoring network evaluates conflict during information processing it signals the need for additional cognitive control, when necessary, to improve subsequent performance. The influence of the cognitive control network is, therefore, thought to vary depending on the level of conflict detected by the conflict monitoring network. Patterns of behaviour during the flanker task demonstrate this theoretical relationship between conflict monitoring and cognitive control. For example, as with many other tasks, after the commission of an error, participants respond slower on the next trial[94,205]. Conversely, when only trials with correct responses are considered,

previous conflict seems to improve performance on subsequent trials: participants respond both faster and more accurately on incongruent flanker trials if they follow an incongruent trial (iI) compared to a congruent trial (cI)[79,82,83,85]. It is thought that the cognitive control network adjusts the strength of its influence based on information received from the conflict monitoring network about ongoing changes in conflict. Therefore, as sources of conflict, flanker incongruence and error commission may contribute to performance variability on subsequent trials by influencing ongoing fluctuations in cognitive control. In support of the purported relationship between conflict monitoring and cognitive control, EEG and fMRI studies have shown that this ACC activity related to conflict or error commission predicts PFC and frontoparietal activity and the magnitude of behavioural adjustment on the following trial[82,90,93–95]. Again, single-trial analysis has shown that higher ERN amplitude is associated with longer reaction time on the subsequent trial providing a link between error-related activity on the previous trial and behavioural performance on the current trial and supporting previous behavioural findings[90]. A similar single-trial analysis using the CRN as a measure of brain activity influenced by conflict may improve our understanding of the dynamic relationship between conflict monitoring, cognitive control, and behaviour.

The primary objective of this study was to examine the relationship between trial-to-trial variability in brain activity and behavioural performance previously shown to be independently related to conflict. Conflict-related brain activity was measured using independent component analysis (ICA) to reveal the response-locked CRN on individual correct trials of a flanker task. To explore our primary objective, the relationship between performance (i.e., reaction time) and single-trial CRN amplitude on the current and previous incongruent trial was examined. It was hypothesized that larger CRN amplitude on the current trial and smaller CRN amplitude on the

previous trial would both be separately associated with longer reaction time on the current trial. Based on the relationship between conflict monitoring and cognitive control, it was also hypothesized that a larger CRN amplitude on the previous trial would be associated with a smaller CRN amplitude on the current trial. A secondary objective was to confirm the influence of previous and current trial conflict, as induced by flanker congruence, on behaviour and examine its influence on our measure of conflict-related brain activity, the single-trial CRN. It was hypothesized that on congruent flanker trials reaction time would be shorter, accuracy would be higher, and CRN amplitude would be smaller than on incongruent trials. It was predicted, however, that if the previous trial was incongruent, reaction time would be shorter, accuracy would be higher, and CRN amplitude would be smaller than if the previous trial was congruent, particularly if the current trial is an incongruent trial (i.e., iI vs. cI trials). Finally, since the CRN and ERN have been shown to share a common neural source, it was predicted that the same independent component selected to reveal the CRN on correct trials would reveal the ERN on error trials, but it was hypothesized that the single-trial CRN would be distinguishable from the single-trial ERN by its smaller amplitude and shorter latency.

5.2 Methods

This study used data previously collected as part of an aerobic exercise study described in Chapter 3. Specifically, this study uses EEG and behavioural data collected during a flanker task performed by participants before they sat quietly on an exercise bike for 35 minutes without pedaling (i.e., before the non-exercise control intervention). The relevant details are included below. The single-trial EEG data processing and statistical analysis described below are unique to this study.

Participants

Sixteen healthy, young adults (8 female) volunteered to participate in this study. This study was approved by the Office of Research Ethics at the University of Waterloo and all participants provided written informed consent before participating. Participants were screened for exclusion criteria including musculoskeletal or neurologic disorders that may have affected their ability to perform the study and their readiness to exercise without requiring permission from their physician (Physical Activity Readiness Questionnaire, Canadian Society for Exercise Physiology, Ottawa, ON).

Experimental protocol

Each participant volunteered to visit the laboratory for three separate sessions: 1) screening and graded exercise test, 2) exercise session, and 3) non-exercise control session. All three sessions are described elsewhere (see Chapter 3). The current study used data from the non-exercise control session only.

Participants started the session seated in a chair in front of a computer monitor. After sitting quietly for two minutes while resting heart rate was measured participants performed four 100-trial blocks of the flanker task for practice. After a four-minute break, participants then performed five more blocks of the flanker task before being seated on the cycle ergometer. Participants sat quietly on the recumbent cycle ergometer for 35 minutes without pedalling and then immediately returned to the chair in front of the computer monitor to perform five more blocks of the flanker task. Only the five blocks immediately before sitting on cycle ergometer were analyzed in the current study.

Flanker task and associated measures

Participants sat in a chair in front of a computer monitor to perform a modified Eriksen flanker task[75,102] delivered via custom software (LabVIEW, National Instruments, Austin, TX). Participants fixated on a point in the center of the screen while stimuli were presented. They began each trial with their hands supported prone on a table in front of them, each thumb resting on a button. In each trial a target stimulus was presented consisting of a right or left pointing arrow (i.e., > or <). The target stimulus was flanked by 4 additional arrows, two on each side, that were either congruent (< < < < < or > > > > >) or incongruent (< < > < < or > > < > >) with the target arrow. Participants responded by pressing a button with their right or left thumb as quickly as possible as indicated by the target arrow. A stimulus was presented for 100ms every 2 seconds and participants were allowed 1500ms to respond. In each block, 25 stimuli of each condition were presented in random order for a total of 100 trials. A voltage output indicating whether the button was pressed or not was sampled at 1,000 Hz and stored for offline processing.

Electromyography. Reaction time was determined from the onset of muscle activity preceding a button press with the thumb. Bilateral flexor pollicis brevis electromyography (EMG) was measured to determine the onset of muscle activity. Electrodes were placed on the muscle belly bilaterally and another electrode was placed on the left ulnar styloid process to act as a ground. Data were amplified (x 500), filtered (10 to 1,000 Hz) (AMT-8, Bortec Biomedical, Calgary, AB), sampled (1,000 Hz), and stored for offline processing.

Electroencephalography. To record brain activity, EEG was recorded from 30 channels using Ag/AgCl electrodes arranged according to the International 10-20 system [190] and embedded into a Lycra cap (Quik-Cap, Compumedics Neuroscan, Charlotte, NC). To record eye

movements and blinks, electrooculography (EOG) was recorded using Ag/AgCl electrodes placed above and below the left eye and lateral to the outer canthus of both eyes. For both EEG and EOG, an electrode at AFz was used as a ground and all electrodes were referenced to the average activity of electrodes located over the left and right mastoid. Impedances for all electrodes were below 5 kΩ. For each block of flanker trials, continuous EEG was amplified (x 19), filtered (DC to 300 Hz), and sampled (1000 Hz) using a Neuroscan amplifier (NuAmps, Compumedics Neuroscan, Charlotte, NC) and software (Scan, Compumedics Neuroscan, Charlotte, NC).

Data processing

EMG signals were bandpass filtered (20-500 Hz), baseline corrected, and full-wave rectified (FWR EMG) before being low-pass filtered (50 Hz; smoothed EMG). FWR and smoothed EMG were used to determine flexor pollicis brevis muscle activity onset using the following criteria: 1) FWR and smoothed EMG must both exceed a threshold equal to the mean plus 3 standard deviations of a 100-ms pre-stimulus baseline and 2) smoothed EMG must remain above this threshold for at least 25 ms.

Each trial was assigned a response status based on the muscle activity and button press response to the stimulus as follows: ‘no response’ when neither button was pressed, ‘correct response’ when only the correct button was pressed, ‘incorrect response’ when only the incorrect button was pressed, ‘remedial response’ when the incorrect button was pressed followed by the correct button, ‘partial incorrect response’ when muscle activity on the incorrect side preceded a correct button press, and ‘undefined’ for any other combination of button presses. Reaction time

was calculated for correct trials only as the time elapsed between stimulus onset and muscle activity onset.

EEG data was band-pass filtered (1 to 100 Hz). Epochs were extracted around the onset of each flanker stimulus (-1000 to 1750 ms) and baseline corrected (-500 to -400 ms). Each epoch was visually inspected and rejected if electrodes contained large amplitude voltage changes indicating noise other than eye artifact. ICA was then performed using the extended Infomax algorithm[191]. Independent components were visually inspected and those representing eye and muscle artifact were removed. Each epoch was visually inspected again for additional noise removal. Electrode voltages were compared to independent component activations to determine if remaining noise could be removed by epoch rejection or independent component rejection.

To examine the single-trial CRN, epochs were created around the appropriate EMG response for correct trials (-1000 to 1000 ms), baseline corrected (-1000 to -800 ms), and band-pass filtered (0.1 to 50 Hz). ICA was performed again on these response-locked epochs. For each participant, a single IC was selected that best resembles the scalp topography and time-course of the CRN. To aid in IC selection, an algorithm was created to rank all ICs based on their activity 50 to 250 ms following EMG onset in correct trials. This algorithm accounted for 1) the amplitude of the negative peak in the component ERP, 2) the correlation of individual trial component activity and FCZ electrode voltage, and 3) the correlation of the component ERP to the FCZ ERP during this time window. From the top 5 ranked ICs, a single IC was selected that had a fronto-central radial topography and a clear negativity following response onset in correct trials [90,195]. This IC was then back-projected to the scalp and examined at the FCz electrode. All EEG data was then band-pass filtered (0.5 to 15 Hz). For each epoch, the negative peak (i.e.,

trough) voltage at the FCz electrode between 0 and 300 ms after EMG onset was identified along with the positive peaks immediately preceding and following. On correct and remedial trials, respectively, CRN and ERN amplitudes were calculated by subtracting the mean of the two positive peaks from the negative peak. CRN or ERN latency was the time from EMG onset to the negative peak voltage. For each epoch, a similar process was used to obtain a baseline peak negativity (800 to 500 ms before EMG onset) along with the positive peaks immediately preceding and following. Amplitude of this baseline peak was also calculated by subtracting the mean of the two positive peaks from the negative peak.

Statistical analysis

To pursue the primary objective, Pearson product-moment correlations were used to examine the associations between CRN amplitude and reaction time within and between trials. For all correlations, both the current and previous trial, if used, were incongruent with a correct response. First, reaction time was plotted against single-trial CRN amplitude on the same trial and the previous trial for each participant and a correlation coefficient was calculated to quantify each of these associations. Next, single-trial CRN amplitude was plotted against CRN amplitude on the previous trial and a correlation coefficient was calculated for each participant. For group analyses of these associations, paired one-sided t-tests were used to compare mean correlation coefficients against zero. To pursue the secondary objective examining the influence of flanker congruence during the current and previous trial on mean response accuracy, reaction time, and CRN amplitude, a repeated-measures analysis of variance (ANOVA) with two factors was used: CONGRUENCE (2 levels: congruent and incongruent) and PREVIOUS CONGRUENCE (2 levels: congruent and incongruent). Finally, separate paired one-tailed t-tests were used to

compare CRN amplitude and latency on incongruent correct trials to that of the ERN on incongruent error trials.

5.3 Results

CRN amplitude

Individual participant correlation between reaction time and CRN amplitude (Figure 5.1) ranged from -0.28 to 0.15 with a mean (sd) of -0.02 (0.11) on the current trial (Figure 5.3) and ranged from -0.22 to 0.40 with a mean of 0.04 (0.14) on the previous trial. Correlation between CRN amplitude on the current and previous trial (Figure 5.2) ranged from -0.13 to 0.25 with a mean of 0.01 (0.10) (Figure 5.3). None of these mean correlations differed significantly from 0 [$t_{(15)}$ = -0.55 to 1.00, p = .167 to .623].

CRN amplitude (Figure 5.4) was -3.94 (3.15) μV on congruent trials and -4.21 (3.80) μV on incongruent trials, a difference of 0.27 μV that was not statistically significant [$F_{(1,15)}$ = 1.99, p = .179]. On incongruent trials immediately following a congruent trial (cI), CRN amplitude was 0.19 μV larger than on those immediately following an incongruent trial (iI), but there was no statistically significant main effect or interaction involving PREVIOUS CONGRUENCE (all F < 0.55, all p > .468).

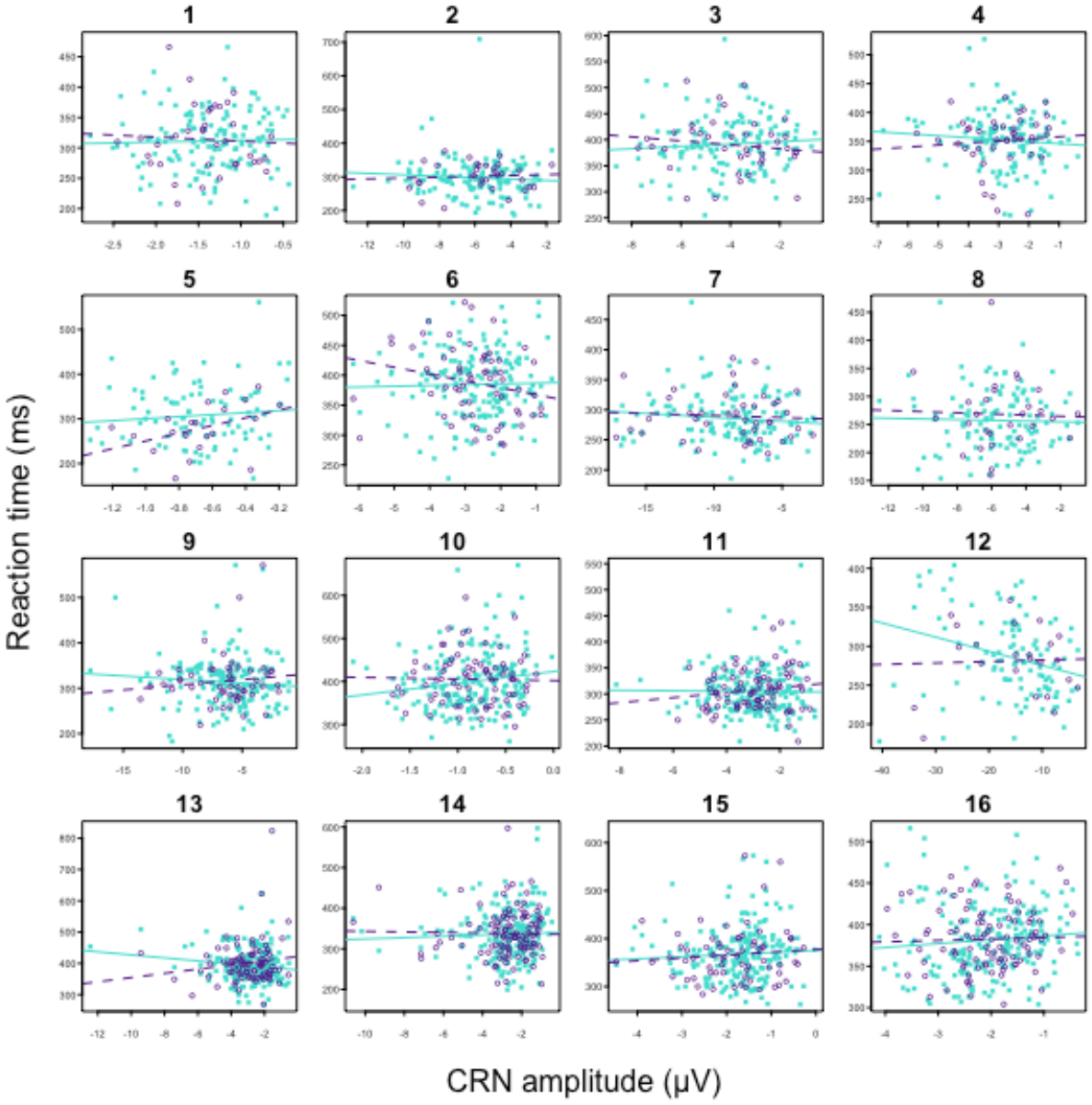

Figure 5.1. CRN amplitude on the current (turquoise filled circles and solid lines) and previous trial (purple open circles and dashed lines) plotted against reaction time for each of the 16 participants. Each point represents a single trial; each line represents a linear model of the data.

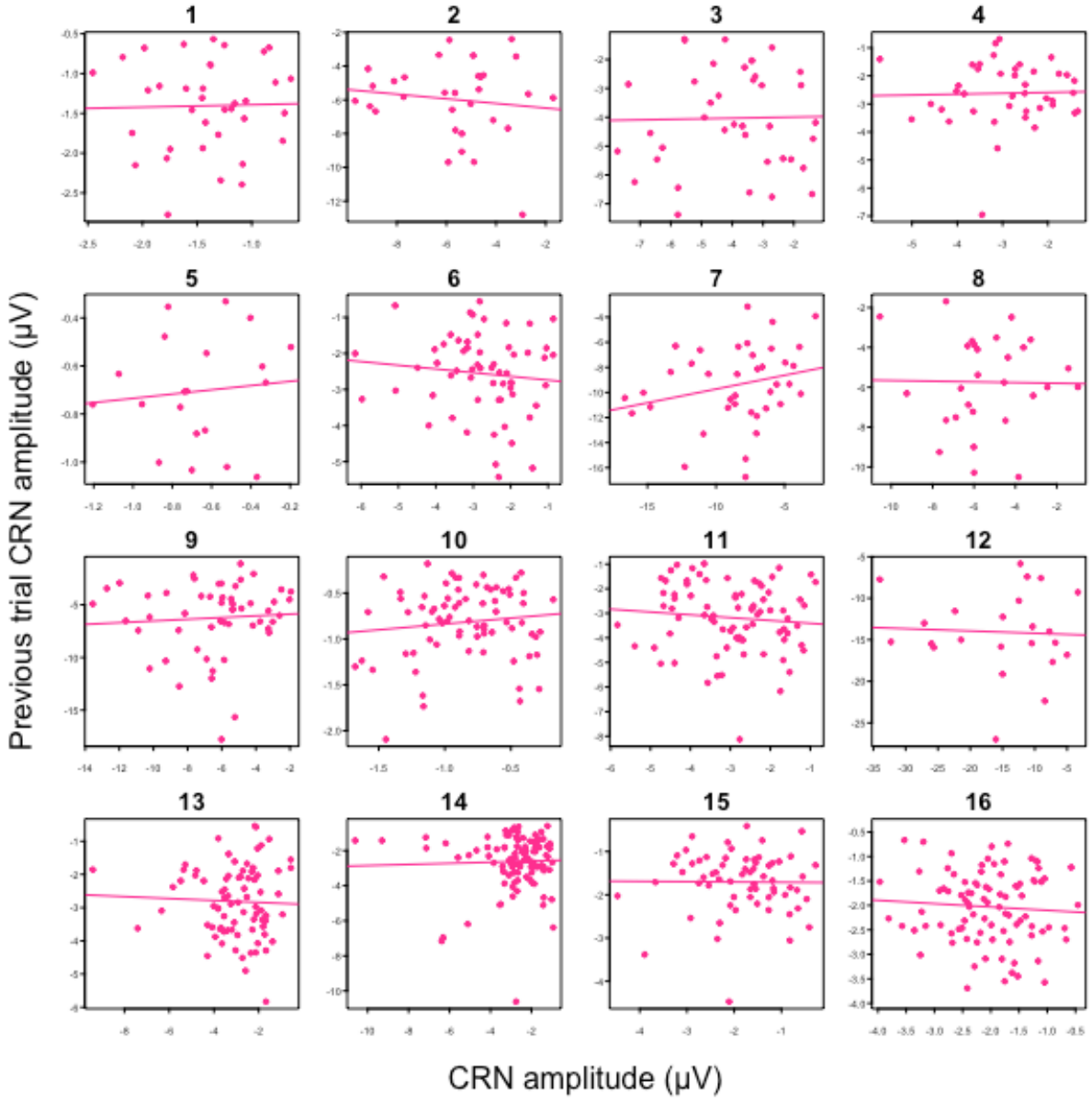

Figure 5.2. CRN amplitude plotted against CRN amplitude on the previous trial for each of the 16 participants. Each point represents a single trial; each line represents a linear model of the data.

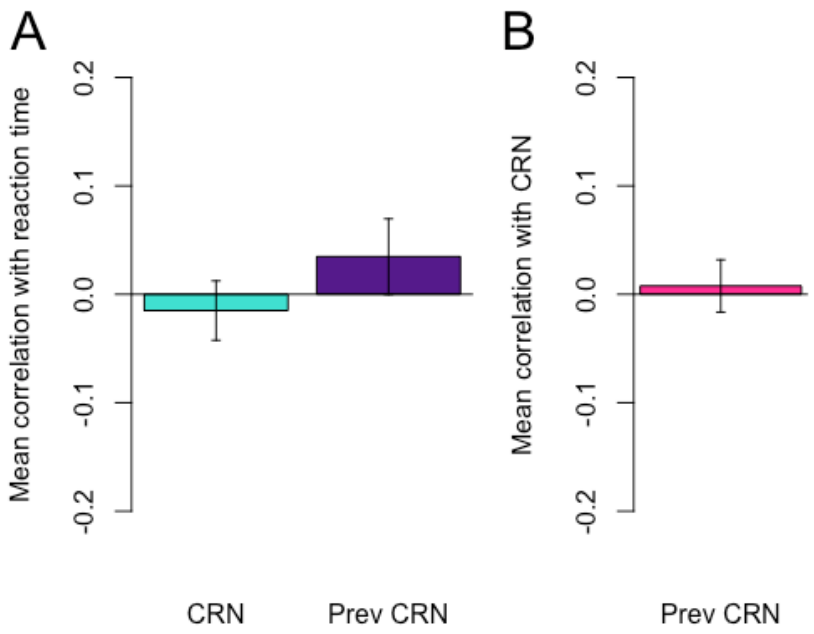

Figure 5.3. Mean Pearson product-moment correlation (mean ± SEM) of reaction time with CRN amplitude on the current and previous trial (A) and of CRN amplitude on the current and previous trial (B).

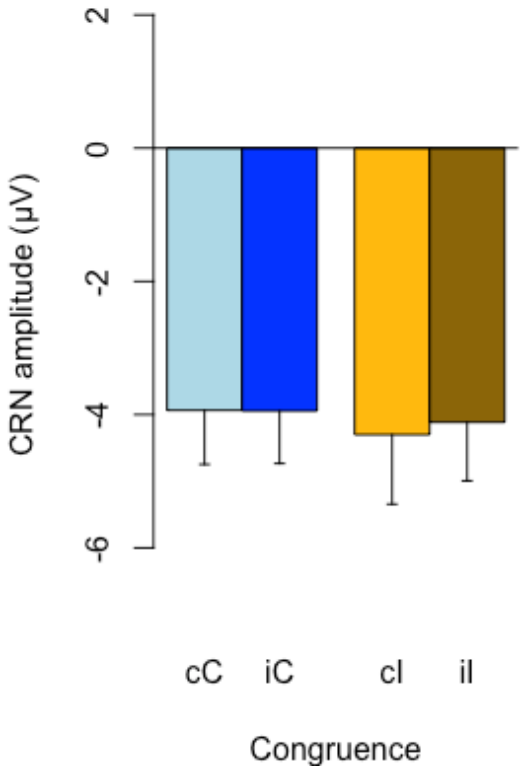

Figure 5.4. Average CRN amplitude (mean - SEM) for each combination of previous (first, lowercase letter) and current trial (second, lowercase letter) flanker congruence (C = congruent, I = incongruent), e.g., cC = congruent previous and congruent current trial.

Reaction time

Mean reaction time (Figure 5.5) was 20.6 ms shorter on congruent than incongruent flanker trials [313.3 (38.1) vs. 333.9 (46.2) ms, $F_{(1, 15)} = 27.12$, $p < .001$]; however, a significant interaction between CONGRUENCE and PREVIOUS CONGRUENCE superseded this main effect [$F_{(1, 15)} = 10.79$, $p = .005$]. Post hoc analysis using two-tailed paired t-tests revealed that, regardless of previous congruence, mean reaction time was always shorter on congruent than incongruent flanker trials (all $p < .003$). Within congruent trials, there was no influence of previous trial congruence on mean reaction time [314.6 (37.7) vs. 311.9 (39.8) ms, $t_{(15)} = 1.68$, $p = .115$]; however, within incongruent trials, mean reaction time was 5.8 ms longer if the previous trial was incongruent (iI) compared to congruent [iC; 331.0 (46.9) vs. 336.8 (46.8) ms, $t_{(15)} = -2.58$, $p = .021$].

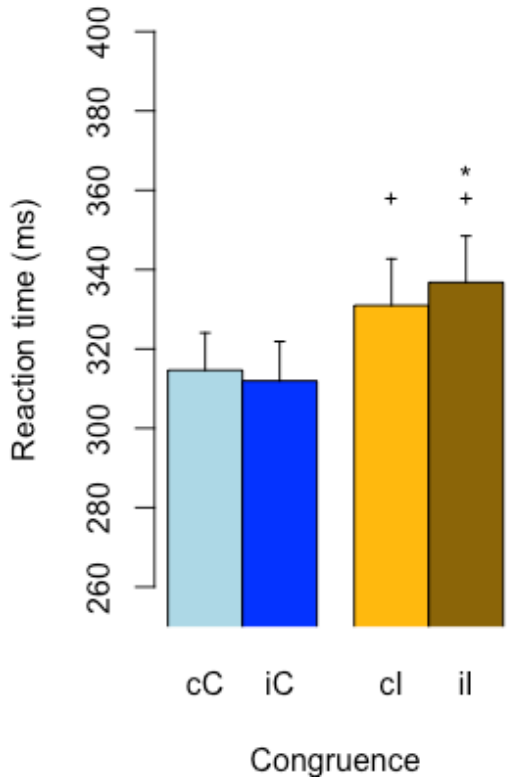

Figure 5.5. Reaction time (mean + SEM) for each combination of previous (first, lowercase letter) and current trial (second, lowercase letter) flanker congruence (C = congruent, I = incongruent). Reaction times on both cI and iI trials were longer than both cC and iC trials (+ all $p < .003$). Reaction time on iI trials was longer than cI trials (* $p = .021$).

Response accuracy

Mean response accuracy (Figure 5.6) was 8.3 % higher on congruent than incongruent flanker trials [97.4 (3.1) vs. 89.1 (9.0) %, $F_{(1, 15)} = 21.10$, $p < .001$]. Collapsed across congruencies, mean response accuracy was also 1.1 % higher when the previous trial was incongruent compared to congruent, but this difference did not reach statistical significance [93.8 (7.8) vs. 92.7 (8.0) %, $F_{(1, 15)} = 4.33$, $p = .055$].

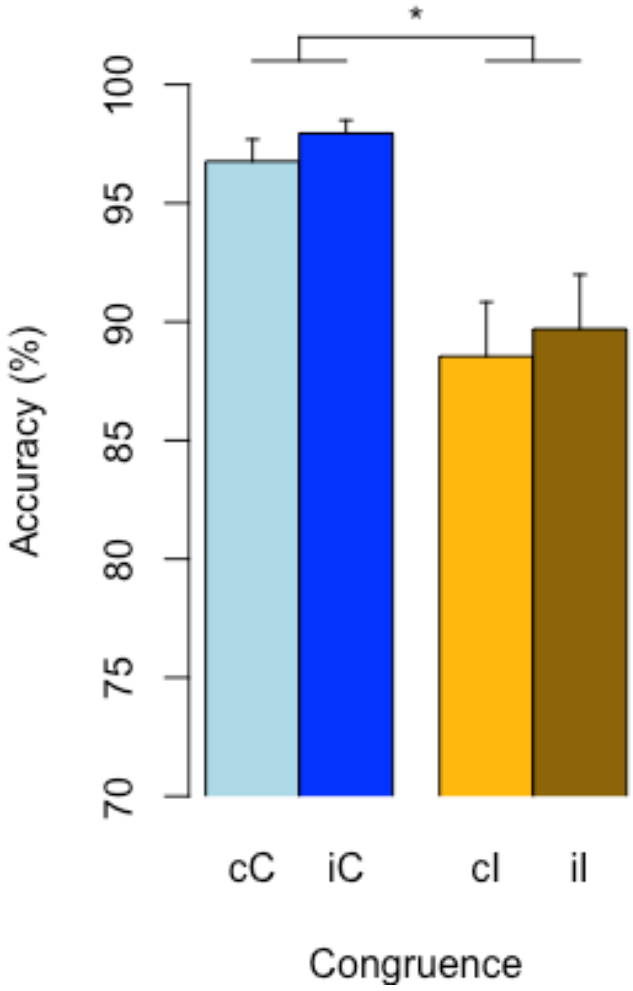

Figure 5.6. Response accuracy (mean + SEM) for each combination of previous (first, lowercase letter) and current trial (second, lowercase letter) flanker congruence (C = congruent, I = incongruent). Response accuracy was higher on congruent than incongruent flanker trials (* $p < .001$).

CRN vs. ERN

Mean ERN amplitude was 1.63 µV larger than CRN amplitude on incongruent trials, but this difference did not reach statistical significance [-5.82 (7.41) vs. -4.19 (3.78) µV, $t_{(15)} = 1.68$, $p = .057$, Figure 5.7A]. Mean ERN latency was significantly longer than CRN latency on incongruent trials [158.9 (43.0) vs. 123.5 (35.2) ms, $t_{(15)} = -4.48$, $p < .001$, Figure 5.7B].

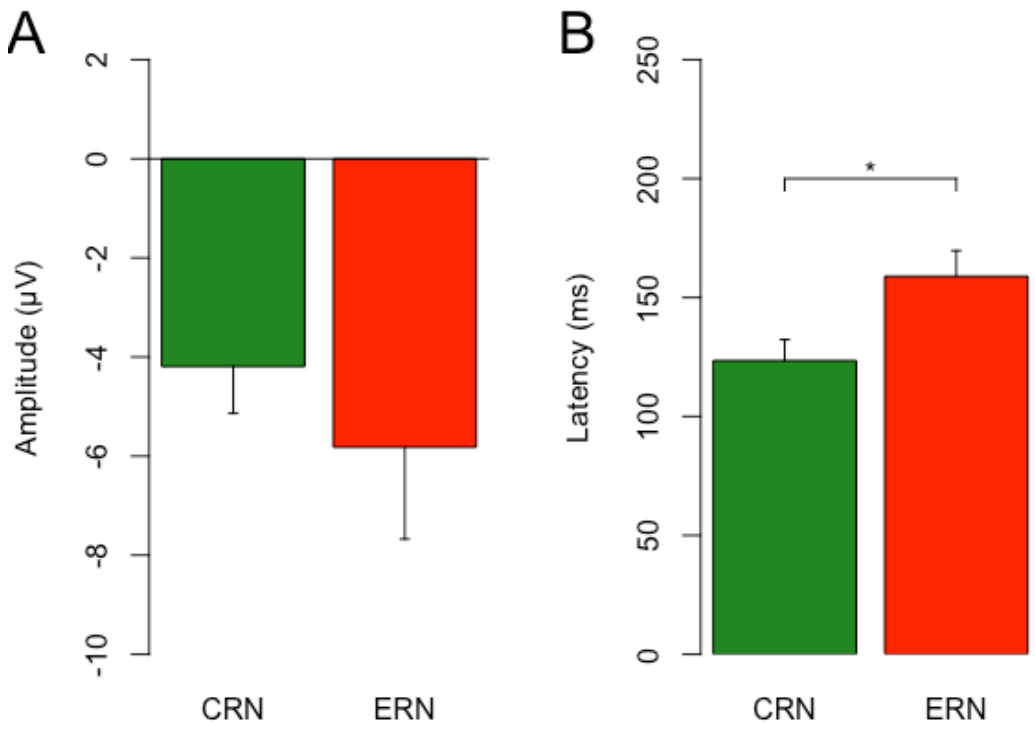

Figure 5.7. CRN and ERN amplitude (A) and latency (B) on incongruent flanker trials. CRN amplitude was smaller than ERN amplitude, but this difference did not reach statistical significance ($p = .057$; A). CRN latency was significantly shorter than ERN latency ($p < .001$; B).

5.4 Discussion

This study set out to examine the relationship between trial-to-trial variability in brain activity (i.e., CRN amplitude) and reaction time as they relate to conflict. It was deemed important to clarify the link between conflict-related brain activity and behaviour before further

examining whether a single session of aerobic exercise impacts the ability of cognitive control to resolve conflict to improve performance during choice reaction tasks. The findings of this study do not support the role of the CRN in monitoring conflict as there was no significant relationship between CRN amplitude and reaction time on the incongruent trials of a flanker task. Instructively, and contrary to previous reports, CRN amplitude did not differ between incongruent and congruent flanker trials defying its purported role in monitoring conflict. Based on these findings, it was not surprising that CRN amplitude on the previous trial was not associated with CRN amplitude or reaction time on the current trial as would be predicted by the relationship between conflict monitoring and cognitive control. Unexpectedly, however, and again contrary to previous reports, response accuracy was higher, but reaction time was longer, on incongruent trials that were preceded by an incongruent compared to a congruent trial. This observation indicates that previous high conflict led to a shift in priority from speed to accuracy, rather an overall performance improvement, indicating that cognitive control may be able implement different strategies to handle increases in conflict. The findings demonstrate the need to further examine the role of the CRN in conflict monitoring and how cognitive control mediates the relationship between conflict and subsequent behavioural change during choice reaction tasks.

During the flanker task, incongruent flankers are purported to cause conflict, the simultaneous activation of multiple response pathways[74], that has been independently associated with both behaviour and brain activity, so the current study examined the relationship between this conflict-related brain activity and concurrent behaviour. Reaction time is longer and response accuracy is lower during incongruent than congruent flanker trials[75,83,86,87,97], so these differences have been attributed to the time taken to resolve this conflict and the increased

likelihood of activating the incorrect response before it is resolved[74,82]. The amplitude of the CRN – a response-locked EEG negativity generated by the ACC – is also larger during incongruent than congruent flanker trials, suggesting its role in monitoring conflict[193,195]. Based on these assertions, it was predicted that, across individual trials, larger CRN amplitude would be associated with longer reaction time. Contrarily, no relationship was found between CRN amplitude and reaction time during incongruent flanker trials. This contradicts a previous single-trial analysis showing that the amplitude of the ERN – also a response-locked negativity generated by the ACC – is related to reaction time during the commission of an error[90]. A potential explanation for this lack of relationship between CRN amplitude and reaction time lies in the disparate influence of flanker congruence on CRN amplitude and reaction time observed in the current study. Similar to previous studies[75,83,86,87,97], reaction time was longer and response accuracy was lower on incongruent than congruent flanker trials. Contrary to previous ERP studies[193,195], however, mean single-trial CRN amplitude did not differ between congruent and incongruent flanker trials. These results coincide with our previous work showing that flanker congruence also did not influence the mean CRN amplitude measured from trial-averaged ERP (see Chapter 4). Taken together, these findings support the assertion that behavioural performance is influenced by conflict but cast doubt upon the role of the CRN, at least as revealed in the current study, in monitoring conflict.

The conflict monitoring network is thought to be involved in the recruitment of cognitive control – when high levels of conflict are detected, additional cognitive control is recruited to reduce conflict and improve performance on subsequent trials[83] – so this study examined how conflict-related brain activity and concurrent behaviour was related to conflict-related brain activity on the previous trial. The dynamic relationship between conflict monitoring and

cognitive control predicts that, during the flanker task, a previous incongruent flanker trial – high in conflict relative to a congruent flanker trial – would result in the recruitment of additional cognitive control that would improve performance on the next trial. Previous observations indicate that reaction time is shorter and response accuracy is higher on incongruent flanker trials if they follow an incongruent trial (iI) than if they follow a congruent trial (cI)[82,83,85]. An extension of this prediction is that a previous trial with a large CRN amplitude – purported to reflect internally-experienced conflict – would recruit additional cognitive control resulting in a smaller CRN amplitude and a shorter reaction time on the subsequent trial. Contrarily, this study found no relationship between CRN amplitude on the previous trial and CRN amplitude or reaction time on the current trial. Again, this finding contrasts with a previous single-trial analysis demonstrating that higher ERN amplitude on the previous trial is associated with longer reaction time on the current trial[90]. It also contradicts previous fMRI studies linking increased conflict-related ACC activity on the previous trial to increased PFC activity and improved performance on the current trial[93,95]. The departure of the current results from those of previous studies may, again, be explained by the lack of an effect of flanker congruence on CRN amplitude in the current study suggesting the CRN is not sensitive to increases in conflict and, therefore, would not be expected to predict conflict-related increases in cognitive control and subsequent improvement in behaviour. Another unexpected result of the current study, however, was that conflict induced by flanker congruence on the previous trial did not influence behaviour or brain activity in the manner predicted by the relationship between conflict monitoring and cognitive control. Rather than an overall performance improvement – shorter reaction time and higher response accuracy – on trials preceded by a high-conflict trial[82,83,85], the current study showed that reaction time was slightly longer and response accuracy was slightly higher on

incongruent trials that were preceded by an incongruent trial compared to those preceded by a congruent trial. Furthermore, CRN amplitude did not differ between incongruent trials preceded by congruent or incongruent trials. Taken together, these results suggest that the relationships between conflict, cognitive control, and performance may be more complicated that previously suggested. At the very least, these findings demonstrate that cognitive control may adopt different strategies to influence performance following high conflict – by shifting priority towards accuracy at the expense of speed or, as previously observed, improving both speed and accuracy. Therefore, the relationship between measures of conflict, such as the CRN amplitude, and performance within and between trials may depend on the cognitive control strategy employed.

While the present findings do not support the purported role of the CRN in monitoring conflict and regulating cognitive control, the single-trial CRN likely reflects activity of the conflict monitoring network even if the meaning of this activity remains unclear. The independent component selected in the current study to reveal the CRN on correct trials also revealed the ERN on error trials suggesting that the source of the CRN is the same as the ERN or similar enough to be indistinguishable by ICA. This coincides with previous research showing that an independent component selected to reveal the ERN also revealed the CRN[195]. This previous work also source-localized both the CRN and ERN to generators within the rostral cingulate zone further supporting their common source within the conflict monitoring network. As predicted, we found that CRN amplitude was smaller than ERN amplitude (although this difference did not reach statistical significance) and CRN latency was shorter than ERN latency. Based on similar findings, previous studies have suggested that the CRN and ERN represent a single ubiquitous response-related cognitive process that is modulated by difference aspects of

performance including, but not limited to, error commission[195]. Further research is needed to explore other potential modulators of this process, including the influence of conflict, and determine how cognitive control strategy may interact with the modulation of this monitoring process.

Finally, methodological differences may explain the departure of the current results from those of previous studies showing an influence of flanker congruence on CRN amplitude. Perhaps the most pertinent differences lie in the EEG processing techniques used to reveal and quantify the CRN. Previous studies demonstrating that the CRN amplitude is larger on incongruent than congruent trials have measured this amplitude from the trial-averaged ERP[193,195] while the current study averaged the mean CRN amplitude obtained from individual trials. This mean single-trial CRN amplitude was also larger on incongruent trials, but the difference was not statistically significant. As well, these previous studies employed cross-trial averaging or a CSD transformation to reveal the CRN, while the current study used ICA to identify a single independent component that represented the CRN. Interestingly, Roger et al.[195] examined the CRN using traditional cross-trial averaging as well as CSD and ICA transformations and found that flanker congruence only influenced the CRN amplitude when revealed using CSD. Further examination of these and other methodological differences between studies examining the CRN should be undertaken to explain the disparity in their results.

5.5 Conclusions

This study did not demonstrate a relationship between brain activity and behaviour purportedly related to conflict. The single-trial CRN employed in the current study to reflect brain activity related to the evaluation of conflict did not differ in amplitude between congruent

and incongruent flanker trials. These findings demonstrate the need to further examine brain activity related to conflict before attempting to determine whether it is influenced by exercise. Unexpectedly, the current study found that conflict on previous trials led to a shift in priority from speed to accuracy rather than an overall performance improvement indicating cognitive control may adopt multiple strategies to adjust performance following high levels of conflict. Future research should, therefore, focus on examining how these results fit with current theories about the integration of conflict monitoring and cognitive control during information processing.

Chapter 6: Discussion

6.1 Summary of research findings

The objective of this dissertation was to examine whether a single session of aerobic exercise impacts the ability of cognitive control to resolve conflict during choice reaction tasks. Much of the presented work was driven by the hypothesis, based on previous data, that aerobic exercise improves performance during specific cognitive tasks by enhancing cognitive control to reduce conflict during information processing[64,65]. The flanker task is a choice reaction task that introduces conflict into information processing by including irrelevant distractor stimuli that may be congruent or incongruent with the target stimulus[75]. The first three studies in this dissertation explored the influence of a single session of aerobic exercise on behavioural performance and electrophysiological (i.e., EEG) markers of conflict during the flanker task. The final study used a subset of this data – before a non-exercise control session – to develop a single-trial measure of conflict-related brain activity and examine the relationship between this activity and conflict-related behavioural change during the flanker task. This study was deemed important as it represents a necessary step toward a better understanding of the dynamic relationship between conflict monitoring and cognitive control and how this relationship may be influenced by exercise.

Behaviourally, the influence of a single session of aerobic exercise on reaction time, movement time, and response accuracy during the flanker task was examined. When electromyography (EMG) onset was used to partition response time into reaction time (i.e., stimulus onset to EMG onset) and movement time (i.e., EMG onset to response completion) aerobic exercise influenced movement time but not reaction time during the flanker task,

regardless of flanker congruence. Movement time was lower before exercise compared to before control, decreased even further during exercise, and quickly increased to pre-exercise levels following exercise. Reaction time, alternatively, decreased similarly over time in both the exercise and non-exercise control conditions suggesting an adaptation over time rather than an influence of exercise. Even after including 400 practice trials, reaction time still decreased 5.5 ms from before to after exercise or non-exercise control (although this decrease was not statistically significant). Exercise had no impact on response accuracy in any of the current studies. Taken together these behavioural findings suggest that aerobic exercise – and even anticipation of exercise – influences the speed of movement-related processes but does not influence the speed of information processing regardless of the requirement for cognitive control.

Using EEG, the influence of aerobic exercise on brain activity of the conflict monitoring network during the flanker task was also examined. Aerobic exercise had no influence on the amplitude of the error-related negativity (ERN) or correct-related negativity (CRN) indicating aerobic exercise does not reduce brain activity related to monitoring conflict caused by error commission or flanker congruence. As well, contrary to previous research, aerobic exercise did not increase P3 amplitude or reduce P3 latency, changes which have been used to support the enhancement of cognitive control following exercise. As with the behavioural findings reported above, these EEG findings also do not indicate any influence of aerobic exercise on cognition, let alone a selective enhancement of cognitive control to reduce conflict.

Finally, the relationship between conflict-related brain activity (i.e., single-trial CRN amplitude) and behaviour (i.e., reaction time) was examined. CRN amplitude was not associated with reaction time on the same trial, and CRN amplitude on the previous trial was not associated with CRN amplitude or reaction time on the current trial. However, CRN amplitude also was not

influenced by flanker congruence on the current or previous trial. Contrary to previous studies, these findings suggest that the brain activity reflected by the CRN may not be related to monitoring conflict induced by incongruent flankers.

Notably, flanker congruence – across all studies – influenced behavioural and electrophysiological variables in a manner consistent with previous studies – reaction time was longer, accuracy was lower, P3 amplitude was lower, and P3 latency was longer during incongruent than congruent trials – supporting the hypothesized increase in conflict and consequent engagement of cognitive control on incongruent flanker trials. However, contrary to previous studies, increased conflict on the previous trial (i.e., iI vs. cI trials) led to slightly longer reaction time and slightly higher response accuracy suggesting that, rather than promoting an overall improvement in performance, increased cognitive control following previous conflict may have led to a shift in priority towards accuracy at the expense of speed.

6.2 Implications for exercise and cognitive control

A single session of moderate intensity aerobic exercise did not influence any behavioural performance or electrophysiological variables in this dissertation that would indicate an improvement in cognitive control. Novel analyses found that a single session of moderate intensity aerobic exercise did not influence brain activity related to conflict caused by error commission or the presence of incongruent distractor stimuli – although these analyses also raised questions about the link between this brain activity and conflict. Furthermore, this dissertation did not replicate any previously observed exercise-induced benefits to behavioural and electrophysiological measures that would indicate improved cognitive function, let alone a specific improvement to cognitive control. It should be noted that numerous controls – many of

which have not been included in previous studies – were included to ensure that previously observed behavioural and electrophysiological changes, as well as those of novel measures of conflict-related brain activity, were indeed indications of a reduction in conflict caused by exercise. Aerobic exercise parameters and cognitive testing time points were selected based on previous meta-analyses that have reported the greatest benefits to cognitive function in the 15-minute window immediately following 20-40 minutes of moderate intensity aerobic cycling exercise[120,121]. These were also consistent with previous studies observing an effect of exercise on cognitive control. As well, a graded exercise test was used to assign a moderate exercise work rate relative to each participant's aerobic fitness. In light of these controls on exercise parameters, it is not likely that the exercise session employed in the current studies was sufficiently different from previous studies to account for the disparities in findings.

Importantly, all behavioural and electrophysiological measures during and after exercise in this dissertation were compared to before exercise and to equivalent time points during a non-exercise control session. As well, response time – often used as a measure of speed of cognitive processing – was partitioned into reaction time and movement time to examine the influence of exercise on cognitive and motor processes, respectively. In study 1, these control measures helped reveal that reaction time during incongruent flanker trials was not influenced specifically by aerobic exercise; instead, it decreased over time regardless of the intervention (i.e., exercise or non-exercise control) suggesting an adaptation effect over time. If this adaptation effect generalizes to other choice reaction tasks, it may explain why larger effects are seen in studies that compare cognitive function before and after exercise but do not include a non-exercise control condition[120]. In study 2, this reduction in reaction time was controlled for by the addition of 400 practice trials and, as a result, neither exercise nor non-exercise control significantly

influenced reaction time. Previous flanker studies have observed shorter response time after exercise than during a baseline or non-exercise control condition[64,65,101,102]. However, these studies only included 20-72 practice trials and did not include a pre-exercise measure, so it is not clear whether adaptation was occurring during the flanker task and how this adaptation interacted with exercise. After including the controls described here, contrary to previous evidence[64,65,101,102], the findings of this dissertation do not support a beneficial effect of a single session of moderate-intensity aerobic exercise on cognitive control in young healthy adults.

Movement time, conversely, was impacted by aerobic exercise – it decreased during exercise and remained slightly shorter immediately after exercise. This finding is consistent with previous research showing a similar effect in simple and choice reaction tasks that coincided with an increase in early EMG activity[137–139]. These findings support TMS work suggesting that aerobic exercise influences primary motor cortex excitability[173]; however, more work is required to localize the source of increased motor unit recruitment during exercise and determine its potential contribution to the observed movement time reduction. Meanwhile, the separable influence of aerobic exercise on reaction time and movement time highlights the importance of partitioning response time as such when examining the effects of aerobic exercise on cognitive function.

Finally, movement time was shorter and CRN amplitude was larger in the exercise session compared to the non-exercise control session at all time points, including before exercise even began. Importantly, participants knew before each session whether or not they were going to exercise – it would not be possible to blind participants to the second session after completing the first – so these effects may result from neurotransmitter modulation linked to increased

arousal or activation in anticipation of exercise[181]. Again, these effects would not have been observed without comparing measures before exercise to a non-exercise control.

6.3 Implications for conflict monitoring and cognitive control

The results of the final study indicate that the CRN does not reflect brain activity related to monitoring conflict generated by irrelevant distractor information. Most importantly, CRN amplitude was not influenced by flanker congruence. This finding contradicts previous suggestions that the CRN reflects the monitoring of conflict created by incongruent flankers[193,195]. Considering this finding, it was not surprising that CRN amplitude was not influenced by flanker congruence on the previous trial and did not predict variability in reaction time or CRN amplitude on the next trial that would arise from conflict-induced regulation of cognitive control[82,83,85]. Again, this differs from previous studies showing that ERN amplitude does vary along with reaction time on error trials and predicts variability in reaction time on the next trial in support of a role in monitoring conflict and influencing adjustments in cognitive control[94,205]. Interestingly, the independent component selected to reveal the CRN on correct trials, however, also revealed the ERN on error trials suggesting the two components share a neural source similar enough to be indistinguishable by ICA. This finding coincides with previous research showing that an independent component selected to reveal the ERN also revealed the CRN[195]. In sum, it appears that the CRN reflects ACC activity related to the evaluation of the response, but it remains unclear exactly what is being evaluated and whether this evaluation is used to regulate cognitive control.

The final study also revealed an unexpected change in behaviour related to flanker congruence on the previous trial. Previous studies have consistently observed a ‘conflict

adaptation' in the form of a reduction in reaction time and increase in accuracy on incongruent flanker trials preceded by an incongruent trial compared to those preceded by a congruent trial[79,82,83,85]. The conflict monitoring model attributes this overall performance improvement to an upregulation of cognitive control caused by the high level of conflict on the previous trial[83]. Rather than an overall performance improvement, however, the final study revealed that a previous incongruent trial led to a longer reaction time and higher response accuracy suggesting a prioritization of accuracy over speed. While this behavioural adjustment differs from previously observed 'conflict adaptation' it is identical to the 'post-error slowing' seen after the commission of an error[94,205].This finding demonstrates that conflict can influence subsequent behaviour in ways other than previously shown. It is possible the specific nature of the behavioural adjustment is based on the goals initially held by the participant such as an emphasis on either speed or accuracy.

6.4 Limitations and future research

This dissertation, along with much of the extant exercise literature, indirectly examined the influence of exercise on cognitive control based on assumptions about the influence of cognitive control on conflict and subsequent behaviour. Emerging neuroimaging studies support these assumptions, but an important next step is to directly examine the influence of exercise on brain activity related to cognitive control. An interesting and novel approach may be to use existing EEG-based techniques, such as independent component analysis (ICA), time-frequency analysis, and network connectivity measures existing EEG-based techniques, to examine the time-varying activity of the cognitive control network within individual trials or across multiple trials. A unique measure of cognitive control capacity may be the responsiveness of this signal to

discrete cortical events purported to specify the need for additional cognitive control, such as the single-trial CRN or ERN employed in this dissertation, and its ability to predict subsequent behaviour. With these, or similar, measures it would then be possible to directly examine the influence of exercise on cognitive control and determine whether previously seen behavioural changes can truly be attributed to enhancement of cognitive control.

The final two studies of this dissertation employed independent component analysis (ICA) of EEG to reveal the CRN. In these studies, a single independent component was selected to represent the CRN based on its scalp topography and time-course of activation. This process is guided by specific spatial and temporal characteristics but is largely subjective. Attempts were made to systematically rank the independent components based on specific quantitative criteria; however, the final selection was made by the researcher. Future work should aim to improve the systematic selection of appropriate independent components for analysis.

Finally, the ability to interpret exercise-induced change in some variables may be limited by the inability to blind the participant to the upcoming intervention. The impact of this limitation was evident by a difference from the control session in some behaviour and EEG measures before exercise even began. It remains unclear how this anticipation effect may influence changes that have been attributed to exercise. It is also not immediately clear how to resolve this limitation, but future research should focus on explaining how and why anticipation of exercise influences cognitive function and behaviour. In the meantime, inclusion of an appropriate non-exercise control condition at least allows consideration of these effects when interpreting results.

It bears noting again that there is growing evidence supporting a beneficial influence of aerobic fitness, long-term aerobic training, and even a single session of aerobic exercise on brain

and cognitive function[53,54,105,106]. While the findings of this dissertation do not support a beneficial effect of a single session of moderate-intensity aerobic exercise on cognitive control in young healthy adults – instead suggesting that inadequate measures of cognitive function and inappropriate control comparisons may have contributed to previously observed performance improvements – generalization of this interpretation is limited to the population, exercise, and cognitive task parameters that were examined in this study.

6.6 Conclusions

The studies in this dissertation were unable to demonstrate a beneficial effect of aerobic exercise on cognitive control but did reveal exercise-induced enhancement of movement-related processes. This dissertation highlighted important methodological considerations when exploring the influence of aerobic exercise on cognitive function including the partitioning of response time into reaction time and movement time and the inclusion of a non-exercise control group. The ability to use independent component analysis to reveal meaningful brain activity on individual trials was also demonstrated; however, these analyses revealed the need to further explore the exact nature of the brain activity revealed by the CRN.

References

1. Botvinick M, Braver T. Motivation and cognitive control: From behavior to neural mechanism. *Annu Rev Psychol*. 2015;66(1):83-113. doi:10.1146/annurev-psych-010814-015044
2. Diamond A. Executive functions. *Annu Rev Psychol*. 2013;64:135-168. doi:10.1146/annurev-psych-113011-143750
3. Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annu Rev Neurosci*. 2001;24(1):167–202.
4. Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cogn Psychol*. 2000;41(1):49-100. doi:10.1006/cogp.1999.0734
5. Banich MT. Executive function: The search for an integrated account. *Curr Dir Psychol Sci*. 2009;18(2):89-94. doi:10.1111/j.1467-8721.2009.01615.x
6. Borella E, Carretti B, Pelegrina S. The specific role of inhibition in reading comprehension in good and poor comprehenders. *J Learn Disabil*. 2010;43(6):541-552. doi:10.1177/0022219410371676
7. Gathercole SE, Pickering SJ, Knight C, Stegmann ZOE. Working memory skills and educational attainment: Evidence from national curriculum assessments at 7 and 14 years of age. *Appl Cogn Psychol*. 2004;16:1-16. doi:10.1002/acp.934
8. St Clair-Thompson HL, Gathercole SE. Executive functions and achievements in school: Shifting, updating, inhibition, and working memory. *Q J Exp Psychol*. 2006;59(4):745-

759. doi:10.1080/17470210500162854

9. Pharo H, Sim C, Graham M, Gross J, Hayne H. Risky business: Executive function, personality, and reckless behavior during adolescence and emerging adulthood. *Behav Neurosci*. 2011;125(6):970-978. doi:10.1037/a0025768

10. Rabin LA, Fogel J, Nutter-upham KE. Academic procrastination in college students: The role of self-reported executive function. *J Clin Expir Neuropsychol*. 2011;33(3):344-357. doi:10.1080/13803395.2010.518597

11. Ready RE, Stierman L, Paulsen JS. Ecological validity of neuropsychological and personality measures of executive functions. *Clin Neuropsychol*. 2001;15(3):314-323.

12. Hinkin CH, Castellon SA, Durvasula RS, et al. Medication adherence among HIV+ adults. *Neurology*. 2002;59:1944-1950.

13. Hall PA, Fong GT, Epp LJ, Elias LJ. Executive function moderates the intention-behavior link for physical activity and dietary behavior. *Psychol Heal*. 2008;23:309-326. doi:10.1080/14768320701212099

14. Cahn-Weiner DA, Boyle PA, Malloy PF. Tests of executive function predict instrumental activities of daily living in community-dwelling older individuals. *Appl Neuropsychol*. 2002;9(3):187-191.

15. Beaudreau SA, O'Hara R. The association of anxiety and depressive symptoms with cognitive performance in community-dwelling older adults. *Psychol Aging*. 2009;24(2):507-512. doi:10.1037/a0016035

16. Snyder HR. Major depressive disorder is associated with broad impairments on neuropsychological measures of executive function: A meta-analysis and review. *Psychol Bull*. 2013;139(1):81-132. doi:10.1037/a0028727

17. Raiker JS, Rapport MD, Kofler MJ, Sarver DE. Objectively-measured impulsivity and attention-deficit/hyperactivity disorder (ADHD): Testing competing predictions from the working memory and behavioral inhibition models of ADHD. *J Abnorm Child Psychol*. 2012;40:699-713. doi:10.1007/s10802-011-9607-2

18. Snyder HR, Kaiser RH, Warren SL, Heller W. Obsessive-compulsive disorder is associated with broad impairments in executive function: A meta-analysis. *Clin Psychol Sci*. 2015;3(2):301-330. doi:10.1177/2167702614534210

19. Aupperle RL, Melrose AJ, Stein MB, Paulus MP. Executive function and PTSD: Disengaging from trauma. *Neuropharmacology*. 2012;62(2):686-694. doi:10.1016/j.neuropharm.2011.02.008

20. Lai M-C, Lombardo M V, Baron-Cohen S. Autism. *Lancet*. 2014;383(9920):896-910. doi:10.1016/S0140-6736(13)61539-1

21. Knowles EEM, Weiser M, David AS, Glahn DC, Davidson M, Reichenberg A. The puzzle of processing speed, memory, and executive function impairments in schizophrenia: Fitting the pieces together. *Biol Psychiatry*. 2015;78(11):786-793. doi:10.1016/j.biopsych.2015.01.018

22. Yakir A, Rigbi A, Kanyas K, et al. Why do young women smoke ? III. Attention and impulsivity as neurocognitive predisposing factors. *Eur Neuropsychopharmacol*. 2007;17:339-351. doi:10.1016/j.euroneuro.2006.09.004

23. Ersche KD, Clark L, London M, Robbins TW, Sahakian BJ. Profile of executive and memory function associated with amphetamine and opiate dependence. *Neuropsychopharmacology*. 2006;31:1036-1047. doi:10.1038/sj.npp.1300889

24. Brand M, Young KS, Laier C. Prefrontal control and Internet addiction: A theoretical

model and review of neuropsychological and neuroimaging findings. *Front Hum Neurosci*. 2014;8:1-13. doi:10.3389/fnhum.2014.00375

25. Ellis JD, Carr MM, Ledgerwood DM. Executive function in problem gamblers with and without history of depression. *Int J Ment Health Addict*. 2017. doi:10.1007/s11469-017-9804-5

26. Azouvi P, Vallat-Azouvi C, Joseph P-A, et al. Executive functions deficits after severe traumatic brain injury : The GREFEX study. *J Head Trauma Rehabil*. 2015;31(3):E10-E20. doi:10.1097/HTR.0000000000000169

27. de Haan EH, Nys GM, Van Zandvoort MJ. Cognitive function following stroke and vascular cognitive impairment. *Curr Opin Neurol*. 2006;19(6):559-564. doi:10.1097/01.wco.0000247612.21235.d9

28. Kirova A, Bays RB, Lagalwar S. Working memory and executive function decline across normal aging, mild cognitive impairment, and Alzheimer's Disease. *Biomed Res Int*. 2015;2015:1-9.

29. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's Dement*. 2011;7(3):270–279.

30. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's Dement*. 2011;7(3):263–269.

31. Salthouse TA. What and when of cognitive aging. *Curr Dir Psychol Sci*. 2004;13(4):140-

144. doi:10.1111/j.0963-7214.2004.00293.x

32. Salthouse TA. When does age-related cognitive decline begin? *Neurobiol Aging*. 2009;30(4):507-514. doi:10.1016/j.neurobiolaging.2008.09.023

33. Salthouse T. Consequences of age-related cognitive declines. *Annu Rev Psychol*. 2012;63(1):201-226. doi:10.1146/annurev-psych-120710-100328

34. Cannon M, T TEM, Caspi A, Murray RM, Harrington H, Poulton R. Neuropsychological performance at the age of 13 years and adult schizophreniform disorder. *Br J Psychiatry*. 2006;189:463-464.

35. Campbell SB, Stauffenberg C Von. Delay and inhibition as early predictors of ADHD symptoms in third grade. *J Abnorm Child Psychol*. 2009;37:1-15. doi:10.1007/s10802-008-9270-4

36. Parslow RA, Ph D, Jorm AF, Ph D, Sc D. Pretrauma and posttrama neurocogntiive functioning and PTSD symptoms in a community sample of young adults. *Am J Psychiatry*. 2007;164:509-515.

37. Zainal NH, Newman MG. Executive function and other cognitive deficits are distal risk factors of generalized anxiety disorder 9 years later. *Psychol Med*. 2017:1-9. doi:10.1017/S0033291717003579

38. Brown TE, Landgraf JM. Improvements in executive function correlate with enhanced performance and functioning and health-related quality of life: Evidence from 2 large, double-blind, randomized, placebo-controlled trials in ADHD. *Postgrad Med*. 2010;122(5):42-51.

39. Biederman J, Fried R, Tarko L, et al. Memantine in the treatment of executive function deficits in adults with ADHD : A pilot-randomized double-blind controlled clinical trial. *J*

Atten Disord. 2017;21(4):343-352. doi:10.1177/1087054714538656

40. Gruber SA, Sagar KA, Dahlgren MK, Gonenc A. The grass might be greener: Medical marijuana patients exhibit altered brain activity and improved executive function after 3 months of treatment. *Front Pharmacol*. 2018;8:1-13. doi:10.3389/fphar.2017.00983

41. Blanco NJ, Maddox WT, Gonzalez-lima F. Improving executive function using transcranial infrared laser stimulation. *J Neuropsychol*. 2017;11:14-25. doi:10.1111/jnp.12074

42. Gill J, Shah-basak PP, Hamilton R. It's the thought that counts: Examining the task-dependent effects of transcranial direct current stimulation on executive function. *Brain Stimul*. 2015;8(2):253-259. doi:10.1016/j.brs.2014.10.018

43. Cheng C, Juan C, Chen M, et al. Different forms of prefrontal theta burst stimulation for executive function of medication-resistant depression: Evidence from a randomized sham-controlled study. *Prog Neuropsychopharmacol Biol Psychiatry*. 2016;66:35-40. doi:10.1016/j.pnpbp.2015.11.009

44. Enriquez-Geppert S, Huster RJ, Herrmann CS. Boosting brain functions: Improving executive functions with behavioral training, neurostimulation, and neurofeedback. *Int J Psychophysiol*. 2013;88(1):1-16. doi:10.1016/j.ijpsycho.2013.02.001

45. Spierer L, Chavan CF, Manuel AL. Training-induced behavioral and brain plasticity in inhibitory control. *Front Hum Neurosci*. 2013;7(August):1-9. doi:10.3389/fnhum.2013.00427

46. Wang JR, Hsieh S. Neurofeedback training improves attention and working memory performance. *Clin Neurophysiol*. 2013;124(12):2406-2420. doi:10.1016/j.clinph.2013.05.020

47. Park DC, Lodi-Smith J, Drew L, et al. The impact of sustained engagement on cognitive function in older adults: The synapse project. *Psychol Sci*. 2014;25(1):103-112. doi:10.1177/0956797613499592

48. Moriguchi Y. The early development of executive function and its relation to social interaction: A brief review. *Front Psychol*. 2014;5(l):1-6. doi:10.3389/fpsyg.2014.00388

49. Bourassa KJ, Memel M, Woolverton C, Sbarra DA. Social participation predicts cognitive functioning in aging adults over time: Comparisons with physical health, depression, and physical activity. *Aging Ment Health*. 2017;21(2):133-146.

50. Hardman RJ, Kennedy G, Macpherson H, Scholey AB, Hardman RJ. Adherence to a Mediterranean-style diet and effects on cognition in adults: A qualitative evaluation and systematic review of longitudinal and prospective trials. *Front Nutr*. 2016;3:1-13. doi:10.3389/fnut.2016.00022

51. Brandmeyer T, Delorme A. Reduced mind wandering in experienced meditators and associated EEG correlates. *Exp Brain Res*. 2016:1-10. doi:10.1007/s00221-016-4811-5

52. Tang Y-Y, Hölzel BK, Posner MI. The neuroscience of mindfulness meditation. *Nat Rev Neurosci*. 2015;16(4):213-225. doi:10.1038/nrn3916

53. Hillman CH, Erickson KI, Kramer AF. Be smart, exercise your heart: exercise effects on brain and cognition. *Nat Rev Neurosci*. 2008;9(1):58-65. doi:10.1038/Nrn2298

54. Prakash RS, Voss MW, Erickson KI, Kramer AF. Physical activity and cognitive vitality. *Annu Rev Psychol*. 2015;66(1):769-797. doi:10.1146/annurev-psych-010814-015249

55. Kokkinos P, Myers J. Exercise and physical activity: Clinical outcomes and applications. *Circulation*. 2010;122(16):1637-1648. doi:10.1161/CIRCULATIONAHA.110.948349

56. Fiuza-Luces C, Garatachea N, Berger NA, Lucia A. Exercise is the real polypill.

Physiology. 2013;28(5):330-358. doi:10.1152/physiol.00019.2013

57. Fox KR. The influence of physical activity on mental well-being. *Public Health Nutr*. 2017;2(3a):411-418. doi:10.1017/S1368980099000567

58. Garber CE, Blissmer B, Deschenes MR, et al. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. *Med Sci Sports Exerc*. 2011;43(7):1334-1359. doi:10.1249/MSS.0b013e318213fefb

59. Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, et al. Exercise and physical activity for older adults. *Med Sci Sports Exerc*. 2009;41(7):1510-1530. doi:10.1249/MSS.0b013e3181a0c95c

60. Karr JE, Areshenkoff CN, Rast P, Garcia-barrera MA. An empirical comparison of the therapeutic benefits of physical exercise and cognitive training on the executive functions of older adults: A meta-analysis of controlled trials. *Neuropsychology*. 2014;28(6):829-845.

61. Kramer AF, Hahn S, Cohen NJ, et al. Ageing, fitness and neurocognitive function. *Nature*. 1999;400:418-419. doi:10.1038/22682

62. Colcombe S, Kramer AF. Fitness effects on the cognitive function of older adults: A meta-analytic study. *Psychol Sci*. 2003;14(2):125-130. doi:10.1111/1467-9280.t01-1-01430

63. Tomporowski PD. Effects of acute bouts of exercise on cognition. *Acta Psychol (Amst)*. 2003;112(3):297-324. doi:10.1016/S0001-6918(02)00134-8

64. Chang Y-K, Pesce C, Chiang Y-T, Kuo C-Y, Fong D-Y. Antecedent acute cycling exercise affects attention control: an ERP study using attention network test. *Front Hum Neurosci*. 2015;9:1-13. doi:10.3389/fnhum.2015.00156

65. O'Leary KC, Pontifex MB, Scudder MR, Brown ML, Hillman CH. The effects of single bouts of aerobic exercise, exergaming, and videogame play on cognitive control. *Clin Neurophysiol*. 2011;122(8):1518-1525. doi:10.1016/j.clinph.2011.01.049

66. Baddeley A. Working memory : Theories, models, and controversies. *Annu Rev Psychol*. 2012;63:1-29. doi:10.1146/annurev-psych-120710-100422

67. Baddeley A. Working memory: Looking back and looking forward. *Nat Rev Neurosci*. 2003;4(10):829–839.

68. Lezak MD. *Neuropsychological Assessment*. 3rd ed. New York: Oxford University Press; 1995.

69. Corsi P. Human memory and the medial temporal lobe region of the brain. *McGill Univ Montr*. 1972.

70. Monsell S. Task switching. *Trends Cogn Sci*. 2003;7(3):134-140. doi:10.1016/S1364-6613(03)00028-7

71. Milner B. Effects of different brain lesions on card sorting: The role of the frontal lobes. *Arch Neurol*. 1963;9:90-100. http://www.usability.gov/how-to-and-tools/methods/card-sorting.html.

72. Stroop JR. Studies of interference in serial verbal reactions. *J Exp Psychol*. 1935;18(6):643-662. doi:10.1037/h0054651

73. Simon JR. Ear preference in a simple reaction-time task. *J Exp Psychol*. 1967;75(1):49-55. doi:10.1037/h0021281

74. van den Wildenberg WPM, Wylie SA, Forstmann BU, Burle B, Hasbroucq T, Ridderinkhof KR. To head or to heed? Beyond the surface of selective action inhibition: A review. *Front Hum Neurosci*. 2010;4(December):222. doi:10.3389/fnhum.2010.00222

75. Eriksen BA, Eriksen CW. Effects of noise letters upon the identification of a target letter in a nonsearch task. *Percept Psychophys*. 1974;16(1):143-149. doi:10.3758/BF03203267

76. Niendam TA, Laird AR, Ray KL, Dean YM, Glahn DC, Carter CS. Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. *Cogntive, Affect Behav Neurosci*. 2012;12:241-268. doi:10.3758/s13415-011-0083-5

77. Vincent JL, Kahn I, Snyder AZ, Raichle ME, Buckner RL. Evidence for a frontoparietal control system revealed by intrinsic functional connectivity. *J Neurophysiol*. 2008;100:3328-3342. doi:10.1152/jn.90355.2008.

78. Spreng RN, Sepulcre J, Turner GR, Stevens WD, Schacter DL. Intrinsic architecture underlying the relations among the default, dorsal attention, and frontoparietal control networks of the human brain. *J Cogn Neurosci*. 2013;25(1):74-86. doi:10.1162/jocn_a_00281

79. Egner T. Congruency sequence effects. *Cogn Affect Behav Neurosci*. 2007;7(4):380-390.

80. Ebitz RB, Hayden BY. Dorsal anterior cingulate: a Rorschach test for cognitive neuroscience. *Nat Neurosci*. 2016;19(10):1278-1279. doi:10.1038/nn.4387

81. DeSoto MC, Fabiani M, Geary DC, Gratton G. When in doubt, do it both ways: Brain evidence of the simultaneous activation of conflicting motor responses in a spatial stroop task. *J Cogn Neurosci*. 2001;13(4):523-536. doi:10.1162/08989290152001934

82. Cohen MX, Cavanagh JF. Single-trial regression elucidates the role of prefrontal theta oscillations in response conflict. *Front Psychol*. 2011;2:1-12. doi:10.3389/fpsyg.2011.00030

83. Botvinick MM, Braver TS, Barch DM, Carter CS, Cohen JD. Conflict monitoring and

cognitive control. *Psychol Rev*. 2001;108(3):624-652. doi:10.1037/0033-295X.108.3.624

84. Shenhav A, Botvinick M, Cohen J. The expected value of control: An integrative theory of anterior cingulate cortex function. *Neuron*. 2013;79(2):217-240. doi:10.1016/j.neuron.2013.07.007

85. Gratton G, Coles MG, Donchin E. Optimizing the use of information: strategic control of activation of responses. *J Exp Psychol Gen*. 1992;121(4):480-506. doi:10.1037/0096-3445.121.4.480

86. Carter CS, Braver TS, Barch DM, Botvinick MM, Noll D, Cohen JD. Anterior Cingulate Cortex, error detection, and the online monitoring of performance. *Science (80-)*. 1998;280(May):747-749.

87. Botvinick M, Nystrom LE, Fissell K, Carter CS, Cohen JD. Conflict monitoring versus selection-for-action in anterior cingulate cortex. *Nature*. 1999;402(6758):179-181.

88. Carter CS, Macdonald AM, Botvinick M, et al. Parsing executive processes: Strategic vs. evaluative functions of the anterior cingulate cortex. *Proc Natl Acad Sci U S A*. 2000;97(4):1944-1948. doi:10.1073/pnas.97.4.1944

89. Yeung N, Botvinick MM, Cohen JD. The neural basis of error detection: Conflict monitoring and the error-related negativity. *Psychol Rev*. 2004;111(4):931-959. doi:10.1037/0033-295X.111.4.931

90. Debener S, Ullsperger M, Siegel M, Fiehler K, von Cramon DY, Engel AK. Trial-by-trial coupling of concurrent electroencephalogram and functional magnetic resonance imaging identifies the dynamics of performance monitoring. *J Neurosci*. 2005;25(50):11730-11737. doi:10.1523/JNEUROSCI.3286-05.2005

91. Cavanagh JF, Zambrano-Vazquez L, Allen JJB. Theta lingua franca: A common mid-

frontal substrate for action monitoring processes. *Psychophysiology*. 2012;49(2):220-238. doi:10.1111/j.1469-8986.2011.01293.x

92. Edwards BG, Calhoun VD, Kiehl K a. Joint ICA of ERP and fMRI during error-monitoring. *Neuroimage*. 2012;59(2):1896-1903. doi:10.1016/j.neuroimage.2011.08.088

93. Kerns JG, Cohen JD, MacDonald AW, Cho RY, Stenger VA, Carter CS. Anterior cingulate conflict monitoring and adjustments in control. *Science (80-)*. 2004;303:1023-1026. doi:10.1126/science.1089910

94. Cavanagh JF, Cohen MX, Allen JJB. Prelude to and resolution of an error: EEG phase synchrony reveals cognitive control dynamics during action monitoring. *J Neurosci*. 2009;29(1):98-105. doi:10.1523/JNEUROSCI.4137-08.2009

95. Walsh BJ, Buonocore MH, Carter CS, Mangun GR. Integrating conflict detection and attentional control mechanisms. *J Cogn Neurosci*. 2011;23(9):2211-2221. doi:10.1162/jocn.2010.21595.Integrating

96. Lu C, Proctor RW. The influence of irrelevant location information on performance: A review of the Simon and spatial Stroop effects. *Psychon Bull Rev*. 1995;2(2):174-207. doi:10.3758/BF03210959

97. Eriksen CW, Schultz DW. Information processing in visual search: A continuous flow conception and experimental results. *Attention, Perception, Psychophys*. 1979;25(4):249–263.

98. Sutton S, Braren M, Zubin J, John ER. Evoked-potential correlates of stimulus uncertainty. *Science (80-)*. 1965;150(3700):1187-1188. doi:10.1126/science.150.3700.1187

99. Polich J. Updating P300: An integrative theory of P3a and P3b. *Clin Neurophysiol*.

2007;118(10):2128-2148. doi:10.1016/j.clinph.2007.04.019

100. Hillman CH, Snook EM, Jerome GJ. Acute cardiovascular exercise and executive control function. *Int J Psychophysiol*. 2003;48(3):307-314. doi:10.1016/S0167-8760(03)00080-1

101. Kamijo K, Nishihira Y, Higashiura T, Kuroiwa K. The interactive effect of exercise intensity and task difficulty on human cognitive processing. *Int J Psychophysiol*. 2007;65(2):114-121. doi:10.1016/j.ijpsycho.2007.04.001

102. Kamijo K, Hayashi Y, Sakai T, Yahiro T, Tanaka K, Nishihira Y. Acute effects of aerobic exercise on cognitive function in older adults. *Journals Gerontol Ser B Psychol Sci Soc Sci*. 2009;64B(3):356-363. doi:10.1093/geronb/gbp030

103. Gehring WJ, Goss B, Coles MGH, Meyer DE, Donchin E. A neural system for error detection and compensation. *Psychol Sci*. 1993;4:385-390. doi:10.1111/j.1467-9280.1993.tb00586.x

104. Falkenstein M, Hohnsbein J, Hoormann J, Blanke L. Effects of crossmodal divided attention on late ERP components. II. Error processing in choice reaction tasks. *Electroencephalogr Clin Neurophysiol*. 1991;78(6):447-455. doi:10.1016/0013-4694(91)90062-9

105. Erickson KI, Hillman CH, Kramer AF. Physical activity, brain, and cognition. *Curr Opin Behav Sci*. 2015;4:27-32. doi:10.1016/j.cobeha.2015.01.005

106. Ballesteros S, Kraft E, Santana S, Tziraki C. Maintaining older brain functionality: A targeted review. *Neurosci Biobehav Rev*. 2015;55:453-477. doi:10.1016/j.neubiorev.2015.06.008

107. Angevaren M, Aufdemkampe G, Verhaar H, Aleman A, Vanhees L. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive

impairment. *Cochrane Database Syst Rev*. 2008;2008(3). doi:10.1002/14651858.CD005381.pub3

108. Lautenschlager NT, Cox KL, Flicker L, et al. Effect of physical activity on cognitive function in older adults at aisk for Alzheimer disease. *J Am Med Assoc*. 2008;300(9):1027. doi:10.1001/jama.300.9.1027

109. Baker LD, Frank LL, Foster-Schubert K, et al. Effects of aerobic exercise on mild cognitive impairment: A controlled trial. *Arch Neurol*. 2012;67(1):71-79. doi:10.1001/archneurol.2009.307

110. Middleton LE, Barnes DE, Lui LY, Yaffe K. Physical activity over the life course and its association with cognitive performance and impairment in old age. *J Am Geriatr Soc*. 2010;58(7):1322-1326. doi:10.1111/j.1532-5415.2010.02903.x

111. Spirduso WW. Reaction and movement time as a function of age and physical activity level. *J Gerontol*. 1975;30(4):435-440. doi:10.1093/geronj/30.4.435

112. Flöel A, Ruscheweyh R, Krüger K, et al. Physical activity and memory functions: Are neurotrophins and cerebral gray matter volume the missing link? *Neuroimage*. 2010;49(3):2756-2763. doi:10.1016/j.neuroimage.2009.10.043

113. Colcombe SJ, Kramer AF, Erickson KI, et al. Cardiovascular fitness, cortical plasticity, and aging. *Proc Natl Acad Sci*. 2004;101(9):3316-3321. doi:10.1073/pnas.0400266101

114. Erickson KI, Prakash RS, Voss MW, et al. Aerobic fitness is associated with hippocampal volume in elderly humans. *Hippocampus*. 2009;19(10):1030-1039. doi:10.1002/hipo.20547

115. Dustman RE, Ruhling RO, Russell EM, et al. Aerobic exercise training and improved neuropsychological function of older individuals. *Neurobiol Aging*. 1984;5(1):35-42.

doi:10.1016/0197-4580(84)90083-6

116. Erickson KI, Voss MW, Prakash RS, et al. Exercise training increases size of hippocampus and improves memory. *Proc Natl Acad Sci*. 2011;108(7):3017-3022. doi:10.1073/pnas.1015950108

117. Smith PJ, Blumenthal JA, Hoffman BM, et al. Aerobic exercise and neurocognitive performance: A meta-analytic review of randomized controlled trials. *Psychosom Med*. 2010;72(3):239-252. doi:10.1097/PSY.0b013e3181d14633

118. Stroth S, Hille K, Spitzer M, Reinhardt R. Aerobic endurance exercise benefits memory and affect in young adults. *Neuropsychol Rehabil*. 2009;19(2):223-243. doi:10.1080/09602010802091183

119. Brisswalter J, Collardeau M, René A. Effects of Acute Physical Exercise Characteristics on Cognitive Performance. *Sport Med*. 2002;32(9):555-566. doi:10.2165/00007256-200232090-00002

120. Lambourne K, Tomporowski P. The effect of exercise-induced arousal on cognitive task performance: A meta-regression analysis. *Brain Res*. 2010;1341(0):12-24. doi:10.1016/j.brainres.2010.03.091

121. Chang YK, Labban JD, Gapin JI, Etnier JL. The effects of acute exercise on cognitive performance: A meta-analysis. *Brain Res*. 2012;1453:87-101. doi:10.1016/j.brainres.2012.02.068

122. Hogervorst E, Riedel W, Jeukendrup a, Jolles J. Cognitive performance after strenuous physical exercise. *Percept Mot Skills*. 1996;83(1971):479-488. doi:10.2466/pms.1996.83.2.479

123. Kubesch, S, Bretschneider, V, Freudenmann, R. Aerobic endurance exercise improves

executive functions in depressed patients. *J Clin Psychiatry*. 2003;64(9):1005-1012.

124. Kashihara K, Nakahara Y. Short-term effect of physical exercise at lactate threshold on choice reaction time. *Percept Mot Skills*. 2005;100(1998):275-291. doi:10.2466/pms.100.2.275-291

125. Aks DJ. Influence of exercise on visual search: implications for mediating cognitive mechanisms. *Percept Mot Skills*. 1998;87(3 Pt 1):771-783.

126. Hogervorst E, Riedel W, Kovacs E, Broun F, Jolles J. Caffeine improves cognitive performance after strenuous physical exercise. *Int J Sports Med*. 1999;20(6):354-361. http://arno.unimaas.nl/show.cgi?fid=7943. Accessed May 23, 2014.

127. Joyce J, Smyth PJ, Donnelly AE, Davranche K. The simon task and aging: Does acute moderate exercise influence cognitive control? *Med Sci Sports Exerc*. 2014;46(3):630-639. doi:10.1249/MSS.0b013e3182a77980

128. Cereatti L, Casella R, Manganelli M, Pesce C. Visual attention in adolescents: Facilitating effects of sport expertise and acute physical exercise. *Psychol Sport Exerc*. 2009;10(1):136-145. doi:10.1016/j.psychsport.2008.05.002

129. Winter B, Breitenstein C, Mooren FC, et al. High impact running improves learning. *Neurobiol Learn Mem*. 2007;87(4):597-609. doi:10.1016/j.nlm.2006.11.003

130. Heckler B. Effects of time of posttest after two durations of exercise on speed and accuracy of addition and subtraction by fit and less-fit women. *Percept Mot Skills*. 1992;75(8):1059. doi:10.2466/PMS.75.8.1059-1065

131. Coles K, Tomporowski PD. Effects of acute exercise on executive processing, short-term and long-term memory. *J Sports Sci*. 2008;26(3):333-344. doi:10.1080/02640410701591417

132. Pesce C, Crova C, Cereatti L, Casella R, Bellucci M. Physical activity and mental performance in preadolescents: Effects of acute exercise on free-recall memory. *Ment Health Phys Act*. 2009;2(1):16-22. doi:10.1016/j.mhpa.2009.02.001

133. Caterino MC, Polak ED. Effects of two types of activity on the performance of second-, third-, and fourth-grade students on a test of concentration. *Percept Mot Skills*. 1999;89(1):245-248. doi:10.2466/pms.1999.89.1.245

134. Davranche K, Hall B, McMorris T. Effect of acute exercise on cognitive control required during an Eriksen flanker task. *J Sport Exerc Psychol*. 2009;31(5):628-639. doi:10.1123/jsep.31.5.628

135. Themanson JR, Hillman CH. Cardiorespiratory fitness and acute aerobic exercise effects on neuroelectric and behavioral measures of action monitoring. *Neuroscience*. 2006;141(2):757-767. doi:10.1016/j.neuroscience.2006.04.004

136. Weng TB, Pierce GL, Darling WG, Voss MW. Differential effects of acute exercise on distinct aspects of executive function. *Med Sci Sport Exerc*. 2015;47(7):1460-1469. doi:10.1249/MSS.0000000000000542

137. Davranche K, Burle B, Audiffren M, Hasbroucq T. Information processing during physical exercise: A chronometric and electromyographic study. *Exp Brain Res*. 2005;165(4):532-540. doi:10.1007/s00221-005-2331-9

138. Audiffren M, Tomporowski PD, Zagrodnik J. Acute aerobic exercise and information processing: Energizing motor processes during a choice reaction time task. *Acta Psychol (Amst)*. 2008;129(3):410-419. doi:10.1016/j.actpsy.2008.09.006

139. Davranche K, Burle B, Audiffren M, Hasbroucq T. Physical exercise facilitates motor processes in simple reaction time performance: An electromyographic analysis. *Neurosci*

Lett. 2006;396(1):54-56. doi:10.1016/j.neulet.2005.11.008

140. Chang Y-K, Chi L, Etnier JL, Wang C-C, Chu C-H, Zhou C. Effect of acute aerobic exercise on cognitive performance: Role of cardiovascular fitness. *Psychol Sport Exerc*. 2014;15(5):464-470. doi:10.1016/j.psychsport.2014.04.007

141. Davey CP. Physical exertion and mental performance. *Ergonomics*. 1973;16(5):595-599. doi:10.1080/00140137308924550

142. Cooper CJ. Anatomical and physiological mechanisms of arousal, with special reference to the effects of exercise. *Ergonomics*. 1973;16(5):601-609. doi:10.1080/00140137308924551

143. Kurosawa M, Okada K, Sato A, Uchida S. Extracellular release of acetylcholine, noradrenaline and serotonin increases in the cerebral cortex during walking in conscious rats. *Neurosci Lett*. 1993;161(1):73-76. doi:10.1016/0304-3940(93)90143-9

144. Pagliari R, Peyrin L. Norepinephrine release in the rat frontal cortex under treadmill exercise: a study with microdialysis. *J Appl Physiol*. 1995;78:2121-2130.

145. Pagliari R, Peyrin L. Physical conditioning in rats influences the central and peripheral catecholamine responses to sustained exercise. *Eur J Appl Physiol Occup Physiol*. 1995;71(1):41-52. doi:10.1007/BF00511231

146. Takatsu S, Ishiwata T, Meeusen R, Sarre S, Hasegawa H. Serotonin release in the preoptic area and anterior hypothalamus is not involved in thermoregulation during low-intensity exercise in a warm environment. *Neurosci Lett*. 2010;482(1):7-11. doi:10.1016/j.neulet.2010.06.073

147. Hasegawa H, Takatsu S, Ishiwata T, Tanaka H, Sarre S, Meeusen R. Continuous monitoring of hypothalamic neurotransmitters and thermoregulatory responses in

exercising rats. *J Neurosci Methods*. 2011;202(2):119-123. doi:10.1016/j.jneumeth.2011.05.024

148. Meeusen R, Smolders I, Sarre S, et al. Endurance training effects on neurotransmitter release in rat striatum: An in vivo microdialysis study. *Acta Physiol*. 1997;159(4):335-341. doi:10.1046/j.1365-201X.1997.00118.x

149. Goekint M, Bos I, Heyman E, Meeusen R, Michotte Y, Sarre S. Acute running stimulates hippocampal dopaminergic neurotransmission in rats, but has no influence on brain-derived neurotrophic factor. *J Appl Physiol*. 2012;112(4):535-541. doi:10.1152/japplphysiol.00306.2011

150. Hattori S, Li QM, Matsui N, Hashitani T, Nishino H. Treadmill running combined with microdialysis to evaluate motor deficits and improvement following dopaminergic grafts in 6-OHDA lesioned rats. *J Neural Transplant Plast*. 1992;3(4):224-224. doi:10.1155/NP.1992.224

151. Hattori S, Naoi M, Nishino H. Striatal dopamine turnover during treadmill running in the rat: Relation to the speed of running. *Brain Res Bull*. 1994;35(1):41-49. doi:10.1016/0361-9230(94)90214-3

152. Hasegawa H, Yazawa T, Yasumatsu M, Otokawa M, Aihara Y. Alteration in dopamine metabolism in the thermoregulatory center of exercising rats. *Neurosci Lett*. 2000;289(3):161-164. doi:10.1016/S0304-3940(00)01276-3

153. Gomez-Merino D, Béquet F, Berthelot M, Chennaoui M, Guezennec CY. Site-dependent effects of an acute intensive exercise on extracellular 5-HT and 5-HIAA levels in rat brain. *Neurosci Lett*. 2001;301(2):143-146. doi:10.1016/S0304-3940(01)01626-3

154. Meeusen R, Thorré K, Chaouloff F, et al. Effects of tryptophan and/or acute running on

extracellular 5-HT and 5-HIAA levels in the hippocampus of food-deprived rats. *Brain Res*. 1996;740(1-2):245-252. doi:10.1016/S0006-8993(96)00872-4

155. Gomez-Merino D, B??quet F, Berthelot M, Riverain S, Chennaoui M, Guezennec CY. Evidence that the branched-chain amino acid L-valine prevents exercise-induced release of 5-HT in rat hippocampus. *Int J Sports Med*. 2001;22(5):317-322. doi:10.1055/s-2001-15645

156. Kail R, Salthouse T a. Processing speed as a mental capacity. *Acta Psychol (Amst)*. 1994;86(2-3):199-225. doi:Cited By (since 1996) 227\rExport Date 21 February 2012

157. Kail R. Developmental change in speed of processing during childhood and adolescence. *Psychol Bull*. 1991;109(3):490-501.

158. Salthouse TA. Aging and measures of processing speed. *Biol Psychol*. 2000;54(1-3):35-54.

159. Salthouse TA. The processing-speed theory of adult age differences in cognition. *Psychol Rev*. 1996;103(3):403-428.

160. Mathias JL, Wheaton P. Changes in attention and information-processing speed following severe traumatic brain injury: a meta-analytic review. *Neuropsychology*. 2007;21(2):212-223. doi:10.1037/0894-4105.21.2.212

161. Chiaravalloti ND, DeLuca J. Cognitive impairment in multiple sclerosis. *Lancet Neurol*. 2008;7(12):1139-1151.

162. Tse C-S, Balota DA, Yap MJ, Duchek JM, McCabe DP. Effects of healthy aging and early stage dementia of the Alzheimer's type on components of response time distributions in three attention tasks. *Neuropsychology*. 2010;24(3):300-315. doi:10.1037/a0018274

163. Sachdev PS, Brodaty H, Valenzuela MJ, et al. The neuropsychological profile of vascular

cognitive impairment in stroke and TIA patients. *Neurology*. 2004;62(6):912-919. doi:10.1212/01.WNL.0000115108.65264.4B

164. van Rooij FG, Schaapsmeerders P, Maaijwee N a M, et al. Persistent cognitive impairment after transient ischemic attack. *Stroke*. 2014;45(8):2270-2274. doi:10.1161/STROKEAHA.114.005205

165. Poels MMF, Ikram M a, van der Lugt A, et al. Cerebral microbleeds are associated with worse cognitive function: the Rotterdam Scan Study. *Neurology*. 2012;78(5):326-333. doi:10.1212/WNL.0b013e3182452928

166. Finkel D, Reynolds CA, McArdle JJ, Pedersen NL. Age changes in processing speed as a leading indicator of cognitive aging. *Psychol Aging*. 2007;22(3):558-568. doi:10.1037/0882-7974.22.3.558

167. Weiss AD. The locus of reaction time change with set, motivation, and age. *J Gerontol*. 1965;20:60-64.

168. Colcombe SJ, Erickson KI, Scalf PE, et al. Aerobic exercise training increases brain volume in aging humans. *J Gerontol Med Sci*. 2006;61A(11):1166-1170.

169. Howley ET, Bassett DR, Welch HG. Criteria for maximal oxygen uptake: review and commentary. *Med Sci Sports Exerc*. 1995;27(9):1292-1301. doi:10.1249/00005768-199509000-00009

170. Borg GAV. Psychophysical bases of perceived exertion. *Med Sci Sport Exerc*. 1982;14(5):377-381. doi:10.1249/00005768-198205000-00012

171. Shvartz E, Reibold RC. Aerobic fitness norms for males and females aged 6 to 75 years: A review. *Aviat Space Environ Med*. 1990;61(1):3-11. http://www.ncbi.nlm.nih.gov/pubmed/2405832.

172. DeLuca CJ. The use of surface electromyography in biomechanics. *J Appl Biomech*. 1997;13(2):135-163. %3CGo%5Cnto.

173. Singh AM, Staines WR. The effects of acute aerobic exercise on the primary motor cortex. *J Mot Behav*. 2015;47(4):328-339. doi:10.1080/00222895.2014.983450

174. Takahashi K, Maruyama A, Hirakoba K, et al. Fatiguing intermittent lower limb exercise influences corticospinal and corticocortical excitability in the nonexercised upper limb. *Brain Stimul*. 2011;4(2):90-96. doi:10.1016/j.brs.2010.07.001

175. Yamaguchi T, Fujiwara T, Liu W, Liu M. Effects of pedaling exercise on the intracortical inhibition of cortical leg area. *Exp Brain Res*. 2012;218(3):401-406. doi:10.1007/s00221-012-3026-7

176. Smith AE, Goldsworthy MR, Garside T, Wood FM, Ridding MC. The influence of a single bout of aerobic exercise on short-interval intracortical excitability. *Exp Brain Res*. 2014;232(6):1875-1882. doi:10.1007/s00221-014-3879-z

177. Singh AM, Duncan RE, Neva JL, Staines WR. Aerobic exercise modulates intracortical inhibition and facilitation in a nonexercised upper limb muscle. *BMC Sports Sci Med Rehabil*. 2014;6(1):23. doi:10.1186/2052-1847-6-23

178. McNeil CJ, Butler JE, Taylor JL, Gandevia SC. Testing the excitability of human motoneurons. *Front Hum Neurosci*. 2013;7(April):152. doi:10.3389/fnhum.2013.00152

179. Singh AM, Neva JL, Staines WR. Acute exercise enhances the response to paired associative stimulation-induced plasticity in the primary motor cortex. *Exp Brain Res*. 2014;232(11):3675-3685. doi:10.1007/s00221-014-4049-z

180. McMorris T, Turner A, Hale BJ, Sproule J. Beyond the catecholamines hypothesis for an acute exercise-cognition interaction: A neurochemical perspective. In: McMorris T, ed.

Exercise-Cognition Interaction: Neuroscience Perspectives. 1st ed. Academic Press; 2015:65-103. doi:10.1016/B978-0-12-800778-5.00004-9

181. McMorris T, Davranche K, Jones G, Hall B, Corbett J, Minter C. Acute incremental exercise, performance of a central executive task, and sympathoadrenal system and hypothalamic-pituitary-adrenal axis activity. *Int J Psychophysiol*. 2009;73(3):334-340. doi:10.1016/j.ijpsycho.2009.05.004

182. McMorris T, Graydon J. The effect of exercise on cognitive performance in soccer-specific tests. *J Sports Sci*. 1997;15(5):459-468. doi:10.1080/026404197367092

183. McMorris T, Myers S, MacGillivary WW, et al. Exercise, plasma catecholamine concentrations and decision-making performance of soccer players on a soccer-specific test. *J Sports Sci*. 1999;17(8):667-676. doi:10.1080/026404199365687

184. Kutas M, McCarthy G, Donchin E. Augmenting mental chronometry: The P300 as a measure of stimulus evaluation time. *Science (80-)*. 1977;197(4305):792-795. doi:10.1126/science.887923

185. Hillman CH, Motl RW, Pontifex MB, et al. Physical activity and cognitive function in a cross-section of younger and older community-dwelling individuals. *Heal Psychol*. 2006;25(6):678-687. doi:10.1037/0278-6133.25.6.678

186. Abernethy B. Dual-task methodology and motor skills research: Some applications and methodological constraints. *J Hum Mov Stud*. 1988;14(3):101-132.

187. Brisswalter J, Durand M, Delignieres D, Legros P. Optimal and non-optimal demand in a dual task of pedalling and simple raction time: Effects on energy expenditure and cognitive performance. *J Hum Mov Stud*. 1995;29:15-34.

188. Dehaene S, Posner MI, Tucker DM. Localization of a neural system for error detection

and compensation. *Psychol Sci*. 1994;5(5):303-305. doi:10.1111/j.1467-9280.1994.tb00630.x

189. Marlin A, Mochizuki G, Staines WR, McIlroy WE. Localizing evoked cortical activity associated with balance reactions: Does the anterior cingulate play a role? *J Neurophysiol*. 2014;(March 2014):2634-2643. doi:10.1152/jn.00511.2013

190. Klem G, Luders H, Jasper H, Elger C. The ten-twenty electrode system of the International Federation. *Electroencephalogr Clin Neurophysiol*. 1958;10(2):371-375. doi:10.1016/0013-4694(58)90053-1

191. Bell AJ, Sejnowski TJ. An information-maximization approach to blind separation and blind deconvolution. *Neural Comput*. 1995;7(6):1129-1159. doi:10.1162/neco.1995.7.6.1129

192. Olvet DM, Hajcak G. The stability of error-related brain activity with increasing trials. *Psychophysiology*. 2009;46(5):957-961. doi:10.1111/j.1469-8986.2009.00848.x

193. Bartholow BD, Pearson MA, Dickter CL, Sher KJ, Fabiani M, Gratton G. Strategic control and medial frontal negativity: Beyond errors and response conflict. *Psychophysiology*. 2005;42(1):33-42. doi:10.1111/j.1469-8986.2005.00258.x

194. Vidal F, Hasbroucq T, Grapperon J, Bonnet M. Is the "error negativity" specific to errors? *Biol Psychol*. 2000;51(2-3):109-128. doi:10.1016/S0301-0511(99)00032-0

195. Roger C, Bénar CG, Vidal F, Hasbroucq T, Burle B. Rostral Cingulate Zone and correct response monitoring: ICA and source localization evidences for the unicity of correct- and error-negativities. *Neuroimage*. 2010;51(1):391-403. doi:10.1016/j.neuroimage.2010.02.005

196. Makeig S, Bell A, Jung T, Sejnowski T. Independent component analysis of

electroencephalographic data. In: Touretzky D, Mozer M, Hasselmo M, eds. *Advances in Neural Information Processing Systems 8*. Cambridge, MA: MIT Press; 1996:145-151.

197. Makeig S, Debener S, Onton J, Delorme A. Mining event-related brain dynamics. *Trends Cogn Sci*. 2004;8(5):204-210. doi:10.1016/j.tics.2004.03.008

198. Jung T-P, Makeig S, Westerfield M, Townsend J, Courchesne E, Sejnowski TJ. Analysis and visualization of single-trial event-related potentials. *Hum Brain Mapp*. 2001;185:166-185.

199. Stokes M, Spaak E. The importance of single-trial analyses in cognitive neuroscience. *Trends Cogn Sci*. 2016;20(7):483-486. doi:10.1016/j.tics.2016.05.008

200. Pernet CR, Sajda P, Rousselet GA. Single-trial analyses: Why bother? *Front Psychol*. 2011;2(NOV):1-2. doi:10.3389/fpsyg.2011.00322

201. Bompas A, Sumner P, Muthumumaraswamy SD, Singh KD, Gilchrist ID. The contribution of pre-stimulus neural oscillatory activity to spontaneous response time variability. *Neuroimage*. 2015;107(0):34-45. doi:10.1016/j.neuroimage.2014.11.057

202. Blankertz B, Lemm S, Treder M, Haufe S, M??ller KR. Single-trial analysis and classification of ERP components - A tutorial. *Neuroimage*. 2011;56(2):814-825. doi:10.1016/j.neuroimage.2010.06.048

203. VanRullen R, Busch NA, Drewes J, Dubois J. Ongoing EEG Phase as a trial-by-trial predictor of perceptual and attentional variability. *Front Psychol*. 2011;2(April):1-9. doi:10.3389/fpsyg.2011.00060

204. Ridderinkhof KR, Ridderinkhof KR, Ullsperger M, et al. The role of the medial frontal cortex in cognitive control. *Science (80-)*. 2004;306(5695):443-447. doi:10.1126/science.1100301

205. Rabbitt PM. Errors and error correction in choice-response tasks. *J Exp Psychol*. 1966;71(2):264-272. doi:10.1037/h0022853