The Acute Effect of Exercise Intensity on Cognitive Function

by

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Recent research has found that regular exercise has a positive effect on cognitive function. Some studies indicate that even an acute session of exercise has a slight positive effect on cognitive function, though factors moderating this effect have not been thoroughly examined. Exercise intensity and timing of cognitive assessment may have an interactive effect on cognitive changes after exercise. Previous research suggests that moderate intensity exercise has the most consistent benefit to cognitive function. In contrast, studies find positive, negative, or null effects to cognitive function after high intensity exercise, where the timing of the post-exercise assessments may account for the observed differences. Since high-intensity interval training (HIIT) is an increasingly popular form of exercise due to equal or greater cardiovascular adaptation for reduced exercise time, understanding its cognitive effects is of interest. The primary objective of the study was to compare the cognitive effects of an acute bout of HIIT to both moderate intensity continuous training (MCT) and rest. The secondary objective was to compare the timeline of the cognitive effects between these three sessions. Twenty-two participants performed 28.5min of HIIT, MCT, and rest on three separate days, each 2 weeks apart. The rest session was performed first and the subsequent exercise sessions were randomized. Cognitive function was assessed using a modified Flanker task with concurrent electroencephalography (EEG) before and 0, 15, 30, and 45min post-intervention. The hypothesis that cognitive function would improve after MCT and HIIT was not supported. Though there was some variability in cognitive function post-exercise, cognitive function was not significantly different before to after exercise or in comparison to the rest session. However, measures of cognitive function were often

better prior to the exercise sessions than before exercise, possibly due to an anticipatory effect prior to exercise or learning carry-over after the rest session, which complicated interpretation of results. Of note, only a small number of prior studies included a baseline assessment of cognitive function in each session. Future research should examine the influence of the anticipation of exercise on cognitive function to better understand whether it is the psychological or physical stress imposed by exercise that enhances cognitive function.

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Table of Contents

List of Figures

List of Tables

List of Abbreviations

AMPA - α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor

BDNF – Brain-derived neurotrophic factor

EEG – Electroencephalography

EOG – Electrooculography

EPSP – Excitatory post-synaptic potential

ERP – Event-related potential

HPA axis - Hypothalamus-pituitary-adrenal axis

HIIT – High intensity interval training

ICV – Intra-individual coefficient of variation

IGF-1 – Insulin-like growth factor 1

IPAQ – International physical activity questionnaire

MCT – Moderate intensity continuous training

NMDA - N-methyl-D-aspartic receptor

PAR-Q – Physical activity readiness questionnaire

RT – Response time

VO_2peak – Peak oxygen uptake

VT – Ventilatory threshold

1. Introduction

Growing evidence supports exercise and physical activity as strategies to improve cognitive function and delay age-related cognitive decline (Kramer & Erickson, 2007). Even a single session (acute bout) of exercise may induce positive changes in cognitive function (Chang, Labban, Gapin, & Etnier, 2012; Lambourne & Tomporowski, 2010). The potential moderators of a single session of exercise are less well understood. This study will probe the influence of exercise intensity (high intensity interval training (HIIT) versus moderate continuous training (MCT)) and the timing of the post-exercise cognitive assessment. Some authors suggest that moderate intensity aerobic exercise induces the greatest cognitive benefit and that high-intensity exercise results in a negative cognitive effect (Kamijo et al., 2004; Kamijo, Nishihira, Higashiura, & Kuroiwa, 2007), but not all research supports this assertion (Hogervorst, Riedel, Jeukendrup, & Jolles, 1996; Magnie et al., 2000). It is possible that the timing of the post-exercise cognitive assessment may, at least partially, account for the differences across studies. A recent meta-analysis suggests that high intensity exercise may have a negative cognitive effect immediately after exercise but a positive effect if measured after a delay (Chang et al., 2012; Lambourne & Tomporowski, 2010); however, this has not been probed within a single study. It may be that high-intensity exercise creates a state of over-arousal responsible for the immediate decrease in cognitive function post-exercise (Dietrich & Audiffren, 2011; McMorris & Hale, 2012). When observed after a delay, the negative effects of over-arousal may be dissipated, resulting in a general improvement of cognitive function some time after high intensity exercise. This literature review will discuss the research examining both the short- and long-term effects of exercise and physical activity on cognitive function. Modifying factors will be examined as well as potential mechanisms.

2. Physical Activity and Cognitive Function

Physical activity has been defined as any bodily movement by skeletal muscle that results in energy expenditure (Neiman, 2003). Exercise is a segment of physical activity that is planned and is designed to improve or maintain physical fitness. Both physical activity and exercise are associated with many health benefits such as decreased risk of stroke, diabetes, coronary heart disease, osteoporosis and various types of cancer (Public Health Agency of Canada, 2012; Brawley et al., 2006). Research also indicates that participation in either a period of exercise training or a single session of exercise is associated with improvements in cognitive function (Chang et al., 2012; Kramer & Erickson, 2007; Lambourne & Tomporowski, 2010). The effect of chronic and acute physical activity and exercise on cognitive function as well as potential effect moderators will be discussed in the following sections.

2.1 Effects of Chronic Physical Activity on Cognitive Function

Maintaining cognitive function is a key component of healthy aging. Maintenance and improvement of cognitive function may be facilitated through physical activity or exercise (Cotman & Berchtold, 2002; Kramer & Erickson, 2007). Many longitudinal studies suggest that habitual physical activity is associated with better brain health and cognitive function, especially in later life (Kramer & Erickson, 2007). Similarly, randomized clinical trials suggest that exercise interventions of 2 to 12 months in length may improve executive function, attention, and visuospatial processes (Colcombe & Kramer, 2003), though results are not entirely consistent and larger, more rigorous trials are needed. The following sections will discuss results from observational studies and clinical trials regarding the effects of chronic physical activity or exercise training on cognitive function.

2.1.1 Cohort Studies

Over the past 20 years, many longitudinal studies have linked physical activity with slower cognitive decline and reduced rates of cognitive impairment and dementia in late life. The first cohort studies supporting the link between physical activity and cognitive outcomes in late life emerged between 1995 and 2001 (Laurin et al. 2001; Yaffe et al. 2001; Yoshitake et al. 1995). One of the earliest studies was an analysis of the Canadian Study of Health and Aging by Laurin et al. (2001). The study recruited over 10,000 Canadians over the age of 65 years. In an analysis of the 4,615 who had normal cognition at baseline, reported physical activity levels, and completed the 5-year follow up, those who were most physically active had lower incidence of Alzheimer's disease, all-cause dementia, and mild cognitive impairment compared to the least active group (Laurin et al., 2001). There was also preliminary evidence suggesting a dose effect where those who had the highest physical activity levels had the lowest rates of cognitive impairment. Since this preliminary work, many additional studies have confirmed these results (Hamer & Chida, 2009; Kramer & Erickson, 2007). Meta-analyses indicate that people who are the most physically active have 45% decreased risk of Alzheimer's disease, 28% decreased risk of all-cause dementia, and 40% decreased risk of vascular dementia compared to those that are the least active (Hamer & Chida, 2009; Verdelho et al., 2012).

The disadvantage of most observational studies is that they rely on self-reported physical activity, which is often not an accurate reflection of true physical activity, especially of non-exercise physical activity (Westertrep, 2009). A few studies have examined the relationship between objective measures of fitness or physical activity and the incidence of cognitive impairment. A longitudinal study by Barnes et al. (2003) examined the relationship between cardiorespiratory fitness and cognitive function among healthy older adults. The study found that

older adults with lower cardiorespiratory fitness had greater cognitive decline over 6 years than the higher fit participants (Barnes, Yaffe, Satariano, & Tager, 2003). Middleton et al., (2011) investigated the relationship of activity energy expenditure, as measured using doubly-labeled water, and the incidence of cognitive impairment. Participants in the highest tertile of activity energy expenditure had 90% lower incidence of cognitive impairment over 3 to 5 years compared to participants in the lowest tertile of activity (Middleton et al., 2011). Buchman et al., (2012) examined the relationship between physical activity, recorded with actigraphy, and the incidence of cognitive decline and Alzheimer's disease. Higher levels of physical activity were associated with lower incidence of both cognitive decline and Alzheimer's disease over the next 4 years (Buchman et al., 2012). These observational studies using objective measures of physical activity and fitness confirm that habitual physical activity is associated with reduced risk of cognitive impairment and dementia.

Despite the growing consensus in observational literature that people with greater habitual physical activity and exercise have lower rates of adverse cognitive outcomes in late life, there are limitations to this research. Most importantly, it remains possible that there are uncontrolled for confounding factors that may explain the relationship between physical activity and cognitive function. The next sections will discuss evidence from clinical trials and experimental studies, which provide stronger evidence for causation.

2.1.2 Randomized Clinical Trials

Randomized clinical trials provide a higher level of evidence for the role of exercise in enhancing cognitive function. Interventions studied have typically ranged from eight weeks to fifty-two weeks in duration with two or three sessions per week (Young, Angevaren, Rusted, & Tabet, 2015). Recent reviews and meta-analyses suggest a small positive effect of exercise on

cognitive function in older populations (Bherer, Erickson, & Liu-Ambrose, 2013; Forbes, Forbes, Blake, Thiessen, & Forbes, 2015; Kramer & Erickson, 2007; Smith et al., 2010; Young et al., 2015), though this effect is not consistent across trials or even across meta-analyses. Two factors that may explain this variability are the cognitive assessments (cognitive domain or task) and, possibly, the exercise dose. Authors also note that methodology of included studies was often poor to moderate and suggested that the minimal effect of exercise on cognitive function might be due to the poor randomization procedures and the high variability in designs, measures, and interventions between studies (Young et al., 2015).

Some cognitive domains seem to be preferentially affected by exercise. One meta-analysis revealed a modest positive effect of regular exercise on attention, executive function, and memory, but not working memory (Smith et al., 2010). In contrast, a meta-analysis by Young et al., (2015) found no effect of regular aerobic exercise on any cognitive domain, only on specific cognitive tests (e.g., verbal fluency, which assesses language and executive function). The discrepancies found between meta-analyses may result from the differing inclusion criteria of each meta-analyses. The latter Cochrane review (Young et al., 2015) only included studies of cognitively healthy adults over 55 years of age that included an assessment of cardiorespiratory fitness whereas Smith et al., (2010) did not have these requirements.

Even though some authors suggest that exercise dose may account for some of the variability between studies (Young et al., 2015), meta-analyses have not found this to be the case. Smith et al., (2010) did find a small positive effect of regular exercise on cognitive function but did not find that exercise dose (intensity or duration) had a significant effect on any of the reported cognitive domains (Smith et al., 2010). Similarly, the Cochrane review found no significant effect for exercise dose on cognitive function (Young et al., 2015). Despite these null

findings, exercise dose may still be influential. Exercise prescription in the reviewed randomized controlled trials was rarely above a moderate intensity so the ability to detect dose-response was limited.

Though most controlled trials have studied older adults, the cognitive benefits of exercise are not limited to elderly populations. A few studies found that exercise training had a positive effect on cognitive function among younger people (Ahamed et al., 2007; Davis et al., 2007; Davis et al., 2011). A 16-month clustered randomized controlled trial of healthy grade four and five children (average age: 10.2 ± 0.6) found that schools that added 15 minutes per day of physical activity had similar academic performance to control schools at follow-up, despite having lower scores before the intervention (Ahamed et al. 2007). More recently, Davis et al. (2011) conducted a randomized controlled trial that randomized 247 overweight children (average age: 9.3 ± 1.0 years) to a high dose group (40 minutes of exercise/day), low dose group (20 minutes/day), or a control group. After 13 weeks, the children assigned to the longer duration exercise intervention had the greatest improvement in both executive function tasks and math tasks. Though effects of exercise may be most observable in older ages, it is evident that regular exercise also has an impact on a young healthy population.

In summary, the breadth of evidence suggests that exercise training is associated with a small cognitive benefit in both early and late life. Attention and executive function may be preferentially affected by exercise, though the effects by cognitive domains are not consistent. Larger, more rigorous studies are needed to provide conclusive evidence for the positive effect of exercise training on cognitive function.

2.2 Effects of Acute Exercise and Cognitive Function

Recent meta-analyses indicate that a single session of aerobic exercise also results in small improvement to cognitive function (Chang et al., 2012; Lambourne & Tomporowski, 2010). These meta-analyses suggest numerous moderators that may alter the cognitive response following exercise, though this effect moderation has often received little attention in individual studies. Potential moderators include exercise intensity, timing of cognitive assessments, and participant fitness levels (Chang et al., 2012).

Exercise intensity may be one of the primary sources of variability between studies (Chang et al., 2012). In a recent meta-analysis, exercise intensities ranging from very light to moderate intensity had a positive effect on cognitive function immediately post-exercise (Chang et al. 2012). In contrast, exercise intensities from light to very high intensity had improved cognitive function when measured after a delay (Chang et al., 2012). The method of intensity classification (for example, heart rate, peak aerobic capacity, and/or ratings of perceived exertion) varied by study; however, the American College of Sports Medicine formally defines exercise intensity ranges as: 1) low intensity exercise: 50-64% of maximum heart rate (HRmax); 2) moderate intensity: 64-77% of HRmax; 3) high (hard) intensity: 77-93% of HRmax; and 4) maximal: 100% of HRmax (American College of Sports Medicine, 2013).

Davey (1973) proposed the inverted-u hypothesis to describe the relationship between acute exercise and cognitive function. This hypothesis is based on the arousal hypothesis which asserts that a state of under or over arousal leads to decreased performance (Yerkes & Dodson 1908). The inverted-u hypothesis suggests that moderate intensity exercise would elicit maximal cognitive benefits and that both low and high intensity exercise would elicit smaller or even negative cognitive effects. A later study by Kamijo et al. (2007) supported this hypothesis in that

light and moderate intensity exercise improved cognitive function, as indicated by decreased stimulus processing time (decreased P300 latency) and increased attentional resources allocated to a task (increased P300 amplitude), but high intensity exercise did not. Similarly, a study by Loprinzi and Kane (2015) found scores on a concentration test increased after an acute bout of moderate intensity exercise when compared to a no-exercise condition. In contrast, neither low nor high intensity exercise induced a significant cognitive change relative to the no-exercise condition (Loprinzi and Kane, 2015). Other studies have also supported this hypothesis, finding that high to maximal intensity exercise had a negative effect on cognitive function (Kamijo et al., 2004; Labelle et al., 2013). However, support for the inverted-U hypothesis is not consistent. Several studies have found a positive cognitive change following an acute session of high intensity exercise (Budde et al., 2012; Hogervorst et al., 1996; Magnie et al., 2000). Magnie et al. (2000) also indicated that attention allocated to a task increases after maximal exercise (increased P300 amplitude) and time to process stimuli decreases (decreased P300 latency). Understanding the influence of high intensity exercise on cognitive function is particularly of interest given its increasing popularity due to strong cardiovascular adaptations and low total exercise time required (Gibala, Little, Macdonald, & Hawley, 2012).

Higher fit or more physically active people may be more likely to experience cognitive benefits after high-intensity exercise. One study of cognitive function during exercise found that variability of performance increased among low fit individuals during high-intensity exercise but not among high fit individuals (Labelle et al., 2013). Another study found that children who reported high physical activity levels had significantly better cognitive performance after exercise compared to after rest (Budde et al. 2012). In contrast, children who reported low

physical activity levels did not. How fitness or habitual physical activity alters the cognitive effects of exercise needs further exploration.

Meta-analyses also suggest that high-intensity exercise benefits cognitive function when assessed after a delay but not when assessed immediately post-exercise (Chang et al., 2012). Studies of the electrophysiological underpinnings of cognitive function also confirm that cognitive function decreases immediately after high intensity exercise (Kamijo et al., 2004; Kamijo et al., 2007) but improves when measured after participants' heart rate values to return to baseline (Hillman, Snook, & Jerome, 2003; Magnie et al., 2000). However, the relationship between exercise intensity and the timing of cognitive effects has not yet been examined within a single study – a topic that the current study will explore.

Only a few individual studies have examined the duration of exercise-induced cognitive changes and these studies have not considered the influence of exercise intensity (Heckler & Croce, 1992; Joyce et al., 2009; Joyce et al., 2014). The first study to examine the duration of cognitive effects recruited a small group of healthy, young women and split them into low and high fit groups (Heckler & Croce, 1992). Participants took part in moderate intensity exercise for one of two durations, 20 or 40 minutes. The participants completed a set of simple math problems immediately, five minutes, and 15 minutes after exercise (Heckler & Croce, 1992). The results indicated that enhanced performance on a simple math task (a measure of crystalized intelligence) lasted up to the final assessment (15 minutes after exercise). This preliminary research demonstrated the facilitative effect of an acute bout of exercise on cognitive function lasted past the immediate post-exercise period. The next study to examine the duration of cognitive effects only used one exercise duration (30 minutes) but assessed cognitive function for a longer period of time, up to 52 minutes after exercise (Joyce et al., 2009). Moderate

intensity exercise was found to increase cognitive performance and, specifically, response inhibition for up to 52 minutes post-exercise (Joyce et al., 2009). More recent research by Joyce et al. recruited young and old participants and assessed their cognitive function before and for 90 minutes after light-moderate intensity exercise (Joyce, Smyth, Donnelly, & Davranche, 2014). In contrast to their previous study, the improvements in cognitive function only persisted 15 to 20 minutes post-exercise and occurred for reaction time but not cognitive control in an executive function task (Joyce et al., 2014). The two studies by this group had similar exercise duration (30min), relative intensity (light-moderate), and cognitive tasks (different tasks, but similar cognitive domains) but different age groups (Joyce et al., 2009; Joyce et al., 2014), where the earlier study used young adults but the latter study used older adults. The duration of cognitive effects may be longer for young adults compared to older adults. Alternatively, it is possible that the lower absolute exercise intensity (despite similar relative intensity) performed by older adults was insufficient to arouse sustained cognitive benefits post-exercise in the latter study (Joyce et al. 2014).

The cognitive effects of exercise also vary by cognitive domain (Chang et al., 2012; Lambourne & Tomporowski, 2010). Although results vary somewhat depending on the timing of the cognitive assessment, acute exercise appears to have minimal effect on information-processing tasks (Chang et al., 2012). In contrast, a larger positive effect after exercise occurs for cognitive tasks probing higher-order cognitive domains including attention and executive function (Chang et al., 2012). Some tasks, such as the Flanker task, include two differing conditions that probe different cognitive functions. The Flanker task includes ‘congruent’ and ‘incongruent’ conditions. Although the tasks will not be discussed in detail in this section, the incongruent condition requires suppression of irrelevant and conflicting stimuli, which probes

the inhibition components of executive function. In contrast, the congruent condition simply requires a quick response to the stimuli, probing information-processing and attention. A number of studies observed a greater positive exercise effect for the more difficult, incongruent trials and a weaker or no effect for the simpler, congruent trials (Hillman et al., 2003; Kamijo et al., 2007; Schmit et al., 2015; Yanagisawa et al., 2010).

Cognitive domain assessed may be another contributing factor to the variable results regarding the influence of exercise dose between studies. In contrast to cognitive effects of exercise in general, it may be that high intensity exercise preferentially affects simple functions (such as information-processing) immediately post-exercise. Kamijo et al., (2007) utilized an executive function task and found high-intensity exercise to be detrimental to stimulus evaluation time (indicated by increased P300 latency). In contrast, Magnie et al., (2000) utilized a simple information-processing task and found high intensity exercise to have a beneficial effect on stimulus evaluation time.

In summary, exercise appears to induce a small positive change in cognitive function that extends for some time post-exercise (Heckler & Croce, 1992; Joyce et al., 2009; Joyce et al., 2014). Though exercise intensity is frequently proposed to alter the effect on cognitive function, the precise role of the dose-response relationship is unclear due to variability in assessments and populations across studies. How the timing and duration of effects varies with exercise intensity, participant fitness, and cognitive domain is an important question that remains to be explored.

3. Potential Mechanisms

The mechanisms that underlie exercise-induced cognitive changes are still unclear. However, the following sections will discuss the potential role of cortisol, catecholamines, brain-derived neurotrophic factor (BDNF), and insulin-like growth factor 1 (IGF-1). It is plausible that

two or more of these mechanisms work together to facilitate exercise-induced changes in cognitive function.

Each of the potential mechanisms share a common effect -- increased glutamate expression (Cotman & Berchtold, 2002; Fernandez & Torres-Aleman, 2012; McEwen, 2007). Glutamate is an excitatory neurotransmitter released by glutamatergic neurons pre-synaptically that acts by binding to N-methyl-D-aspartic (NMDA) and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA) receptors on the post-synaptic membrane (Cotman & Berchtold, 2002; McEwen, 2007). Once bound, NMDA and AMPA receptors open, allowing for an influx of positive sodium and calcium ions creating excitatory post-synaptic potentials (EPSPs), thereby increasing the likelihood of action potential propagation due to summation of EPSPs in cognitive networks among others.

An increase in EPSPs may alter both the rate of neuronal firing and the total neural activation. Behaviorally, an increased rate of neuronal firing may translate to an improved response time, and an increase in neural activation may translate to improved response accuracy (Luck, 2005). Electrophysiologically, this may be observed through fluctuations in dipoles. A dipole refers to the difference in electrical charge within a neuron (Luck, 2005). A dipole change is reflective of the electrical activity within that neuron, however not all dipoles reflect action potential propagation as not all EPSPs sum to create an action potential. EEG is a useful technique for recording dipole activity to provide a deeper insight into EPSP fluctuations (see section 4.2 for further discussion on EEG). In particular, P300 amplitude and latency can be analyzed to observe the average dipole activity and the rate of dipole fluctuations respectively. Analysis of this waveform may be a useful indication of neural changes.

Exercise has been demonstrated to globally increase glutamate availability in the brain, this increase in glutamate would be reflected in P300 amplitude and latency through the above mentioned pathways (Maddock, Casazza, Fernandez, & Maddock, 2016). The mechanisms described act to either initiate the increased availability of glutamate or take advantage of the increased availability of glutamate.

3.1 Cortisol

Cortisol is a glucocorticoid hormone produced by the adrenal gland. Cortisol is released in response to a stressor. The primary function of cortisol is to modulate the release of corticosteroids produced in the hypothalamus-pituitary-adrenal (HPA) axis. Specifically, cortisol is thought to modulate arousal by limiting the production of corticotrophin releasing hormone and adrenocorticotrophin hormone in order to return the HPA axis functioning to pre-stress levels (Lambourne & Tomporowski, 2010; McEwen, 2007).

It is thought that hormones released by the adrenal gland (including cortisol) contribute to synaptic plasticity (McEwen, 2007), particularly in the prefrontal cortex (Radley, Morilak, Viau & Campeau, 2015). Cortisol and other corticosteroids released by the HPA axis bind to neuronal receptors pre-synaptically, which leads to a cascade of interactions within the neuron resulting in the release of glutamate from the pre-synaptic neuron into the synapse (McEwen, 2007). This increase in glutamate will drive an influx of positive ions into the post-synaptic neuron, thereby creating an EPSP and increasing the likelihood of action potential propagation (Cotman & Berchtold; McEwen, 2007), as discussed above.

Aerobic exercise can be considered a stressor and elicits the expected stress response from the HPA axis (Mastorakos, Pavlatou, Diamanti-Kandarakis, & Chrousos, 2005; McMorris, Collard, Corbett, Dicks, & Swain, 2008). Deuster et al. (1989) found a strong correlation

between exercise intensity and cortisol release, measured through salivary cortisol levels. Cortisol was released in proportion to exercise intensity, where high intensity exercise elicited the greatest cortisol release (Deuster et al., 1989). Though much research has focused on the impact of stressor intensity on cortisol release, the impact of cortisol levels on cognitive function has remained relatively unexplored. Recent research has proposed that cortisol may influence working memory in an inverted-u function (Moriarty et al., 2014; Schilling et al., 2013). Moderate levels of cortisol were correlated with higher performance on both spatial working memory tasks and image recall tasks compared to high or low levels of cortisol. Further research is required to determine the impact of cortisol on different cognitive domains and different components of executive function including response inhibition.

The duration of the effects of exercise on cortisol also appears to be influenced by exercise intensity. Cortisol has been found to be present peripherally for up to 2 hours after both moderate and intense exercise (Duclos et al., 1998; Labsy et al., 2013). Of note, the extended duration of exercise in prior studies (>90 min) may have contributed to the prolonged elevation of cortisol (Duclos et al., 1998; Labsy et al., 2013). Further research is required to elucidate the precise timeline of the cortisol response to varying durations and intensities of exercise.

3.2 Catecholamines

Though the modulation of the HPA axis by cortisol is important to the stress response, it has been suggested that catecholamines (specifically norepinephrine and epinephrine) and their influence on the sympathetic system are more sensitive to exercise intensity (Deuster et al., 1989). Similarly to cortisol, catecholamines are released by the adrenal gland in response to stress (McMorris et al., 2008; Skosnik, Chatterton, Swisher, & Park, 2000; Skriver et al., 2014; Winter et al., 2007). Increases in catecholamine levels, including those induced by stress, are

strongly correlated with increased cognitive performance up to a threshold (Skosnik et al., 2000; Winter et al., 2007). Excessive catecholamine levels are thought to be detrimental to cognitive function (Cooper et al., 1973). Although the mechanisms in brain linking catecholamines to cognitive function are not well examined, peripherally epinephrine and norepinephrine have a critical role in initiating many of the physiological responses to stress. It has been suggested that catecholamines may act similarly to cortisol by binding to pre-synaptic receptors and increasing the release of glutamate at the synapse (McEwen, 2007).

There is also some evidence that the catecholamine response to exercise may be related to exercise intensity, where the increase in catecholamines is greater with higher exercise intensity (Deuster et al., 1989; McMorris et al., 2012; Winter et al., 2007). In line with the inverted-U hypothesis, it has been suggested that moderate intensity exercise may result in optimal release of catecholamines for cognitive benefits whereas minimal increases with low intensity and excess amounts with very high intensity have a null or negative effect on cognitive function (Cooper et al., 1973; Deuster et al., 1989; McMorris & Hale, 2012; Winter et al., 2007). However, not all studies find a correlation between change in catecholamine levels after exercise and change in cognitive performance (Winter et al., 2007; Segal, Cotman & Cahill, 2012). The reason for the inconsistency in results is unclear. It may be related to the timing of assessments, where catecholamine levels are likely to decrease with time post-exercise. After high intensity exercise, it may be that catecholamine levels are too high immediately after exercise but that excessive catecholamine levels would likely pass through the 'optimal' range before returning to rest levels post-exercise. As a result, it is likely that there is a point of augmented cognitive function due to the rise in catecholamines after high-intensity exercise. Further examination is required to determine the time point at which arousal will be at this optimal level.

Most research investigating the links between exercise, catecholamines, and cognitive function have focused on the role of epinephrine and norepinephrine. Peripheral levels of epinephrine and norepinephrine are consistently higher post-exercise (Galbo, Holst & Christensen, 1975; Peyrin, Pequignot, Lacour, & Fourcade, 1987; Skriver et al., 2014; Winter et al., 2007). A strong correlation between exercise intensity and peripheral levels of epinephrine has been found with high intensity exercise eliciting the greatest increase in peripheral epinephrine (Peake et al., 2014; Winter et al., 2007), though this finding is not consistent across all studies (Deuster et al., 1989). In contrast, peripheral norepinephrine seems to be less sensitive to exercise intensity than epinephrine. Peake et al. (2014) found no significant difference to exist between high and moderate intensity levels of peripheral norepinephrine post exercise (Peake et al., 2014). Although we cannot assume that central levels of catecholamines mimic peripheral increase, there is some evidence that peripheral increases in epinephrine are correlated with increases in norepinephrine in the brain after exercise (Pagliari & Peyrin, 1995). Furthermore, one study in animals found that cortical norepinephrine was elevated 30 minutes after 1 hour of exercise and for 70 minutes after 2 hours of exercise (Pagliari & Peyrin, 1995). However, it is not yet clear how long the elevation in catecholamines lasts, though a trend towards baseline levels was already evident within this study.

3.3 Growth Factors

Several growth factors may contribute to the acute cognitive changes post-exercise. This section will discuss two growth factors likely to contribute to exercise-induced cognitive change: insulin-like growth factor (IGF-1) and brain-derived neurotrophic factor (BDNF) (Cotman & Berchtold, 2002; Skriver et al., 2014; Tonoli et al., 2015; Winter et al., 2007). Importantly, the

two are interrelated, where IGF-1 is thought to be a mediator of BNDF regulation in the brain (Cotman & Berchtold, 2002; Fernandez & Torres-Aleman, 2012).

BDNF is thought to have a significant role in the cognitive response to exercise (Cotman & Berchtold, 2002), especially the chronic response to training but also the acute response to a single session of exercise. To date, research regarding the central changes in BDNF in response to exercise has been limited to chronic effects. The acute effects of exercise on BDNF levels are less well understood; however, there is some evidence that BDNF may at least partially underlie the acute cognitive effects experienced post-exercise. A recent review of the influence of exercise on peripheral BDNF levels suggests that BDNF increases after acute exercise in a dose-dependent manner (Knaepen et al., 2010) but results from individual studies are highly variable (Skriver et al., 2014; Tonoli et al., 2015; Winter et al., 2007).

There is some evidence that post-exercise elevations in BDNF are associated with cognitive benefits. One study suggested that the elevation in peripheral BDNF levels post-exercise were associated with improved learning and long-term memory (Winter et al., 2007). Another study indicated that increased levels of both BDNF and IGF-1 are associated with increased executive function performance on the Stroop task (Tonoli et al., 2015). These results suggest that BDNF may have a role in improving cognitive function post-exercise.

It is reasonable to think that BDNF could be responsible for cognitive changes. BDNF is thought to acutely augment both the pre-synaptic release of glutamate as well as post-synaptic sensitivity, both of which may enhance neuronal firing (Cotman, Berchtold, & Christie; 2007; Knaepen et al., 2010; Leßmann, 1998; Rose, Blum, Kafitz, Kovalchuk, & Konnerth, 2004). Pre-synaptically, BDNF increases glutamate release into the synapse though the precise cellular mechanism through which this occurs is unknown (Leßmann, 1998; Rose et al., 2004). Post-

synaptically, BDNF has been theorized to act as an ion channel modulator and, in some cases, may act as an excitatory neurotransmitter (Rose et al., 2004). BDNF binds to the TrkB receptors at the post-synaptic membrane, thereby initiating a signaling cascade within the cell. The long-term effects of this cascade contribute to both axon growth and long-term potentiation. Acutely, this cascade causes an increase in synaptic transmission through the modulation of ion channels allowing an influx of positive ions through the post-synaptic membrane (Cotman & Berchtold, 2002; Rose et al., 2004). The resultant influx of positive ions accumulates to create EPSPs and increases the likelihood of an action potential.

IGF-1 may also underlie the cognitive effects seen after exercise, particularly through the impact of peripheral IGF-1 on central BDNF. Though IGF-1 is predominantly produced peripherally, it may still be an important contributor to the cognitive response to exercise through its ability to cross the blood brain barrier (Fernandez & Torres-Aleman, 2012; Knaepen et al., 2010). IGF-1 is considered to be a mediator of BDNF regulation in the brain and, therefore, could contribute to improved cognitive performance through enhanced neuronal firing (Cotman & Berchtold, 2002; Fernandez & Torres-Aleman, 2012). In addition to the role of IGF-1 as an upstream mediator of BDNF regulation, it has been suggested that IGF-1 may bind to the pre-synaptic neuron and induce the release of glutamate at the synapse thereby initiating the cascade of events responsible for action potential propagation. IGF-1 may also bind to post-synaptic receptors, allowing the influx of positive ions and ultimately increasing the likelihood of action potential conduction at the neuron (Fernandez & Torres-Aleman, 2012).

Increasingly, IGF-1 has become an area of focus for research exploring the potential mechanisms through which acute exercise may influence cognitive function. IGF-1 has been found to increase post-exercise (Knaepen et al., 2010; Skriver et al., 2014) with some studies

suggesting that the increase in IGF-1 is greater with higher intensity exercise (Schwarz, Brasel, Hintz, Mohan, & Cooper, 1996, Tonoli et al., 2015). The specific timeline of IGF-1 release after exercise is unknown and requires further investigation.

4. Assessments of Executive Function

This study will focus on the effects of exercise on executive function, though attention and information processing are also captured by the assessment used (modified Flanker task, discussed in detail in Section 4.1). Executive function refers to a group of complex cognitive processes that include but are not limited to inhibition, working memory, and mental set shifting (Miyake et al., 2000). Inhibition involves the suppression of dominant responses to achieve a goal-directed behavior. Mental set shifting refers to the ability to engage and disengage between appropriate tasks or behaviors (Miyake et al., 2000). Working memory involves the process of monitoring incoming stimuli for task-relevance and then modifying stored material by replacing irrelevant information with newer, more relevant information (Miyake et al., 2000). In contrast to information-processing, executive function processes do not become automatic over time (Hommel, Ridderinkhof & Theeuwes, 2002; Miyake et al., 2000).

Executive function processes are often accompanied by activation of the frontal and prefrontal cortex (Fallgatter & Strik, 1998a; Miyake et al., 2000; Yanagisawa et al., 2010). Activation in the dorsolateral prefrontal cortex (DLPFC), in particular, is associated with cognitive tasks requiring response inhibition (Schmit et al., 2015; Yanagisawa et al., 2010). Previous research indicates that executive function is susceptible to age-related cognitive decline; therefore, strategies to maintain executive function throughout the life course are essential (Davidson, Zacks, & Williams, 2003).

Recent meta-analyses indicate an overall small positive effect of exercise on executive function (Chang et al., 2012; Lambourne & Tomporowski, 2010). However, the effect varies by assessment. The magnitude of the effect on executive function following an acute exercise session may be modified by the type of measure, timing of assessment, and exercise intensity, as discussed above. Measures of executive function to be employed in this study are discussed in the following sections.

4.1 Behavioural Measures

The modified Flanker task appears to be sensitive to exercise effects (Hillman et al., 2003; Kamijo et al., 2007; Kamijo et al., 2009; Peiffer, Darby, Fullenkamp, & Morgan, 2015; Schmit et al., 2015). The modified Flanker task also has the advantage of being readily paired with electroencephalography (EEG) to create event related potentials (ERPs), as discussed below. For these reasons, a modified Flanker task will be used to assess cognitive function in this study.

This modified Flanker task employed in this study consists of two conditions (congruent and incongruent). For both types of trials, a series of arrows are displayed to the participant. If the direction of the centre arrow matches the direction of the surrounding arrows (e.g. >>>>>), it is a congruent trial. If the direction of the centre arrow does not match the surrounding arrows (e.g. >><>>), it is an incongruent trial. The interference effect refers to the increased response time required for incongruent trials relative to congruent trials (Eriksen & Eriksen, 1974). The simpler, congruent trials assess both attention and information-processing and the more difficult, incongruent trials assess information-processing as well as response inhibition, an aspect of executive function (Eriksen & Eriksen, 1974).

In this study, performance on the modified Flanker task was assessed using response time, though accuracy can also be quantified. Response time refers to the period of time between stimulus presentation and a behavioural response, in this case a button press. Accuracy refers to the percentage of responses that are correct. Response time is often more sensitive to exercise interventions than accuracy (Hillman et al., 2003; Kamijo et al., 2007; Schmit et al., 2015; Yanagisawa et al., 2010), perhaps because accuracy tends to be high so there is insufficient variability to detect an exercise-induced change.

4.2 Electroencephalography

EEG is a non-invasive technique used to record brain activity with high temporal resolution (ms), but low spatial representation (Picton et al., 2000). EEG can be paired with cognitive tasks to reflect the underlying cortical activity. ERP is one type of analysis that time-locks EEG to an event (e.g. task stimuli) to observe associated electrophysiological changes. EEG primarily records the cumulative changes in EPSPs of the most superficial neurons. ERPs can be compared as average changes in electrical activity in the most superficial neurons before or after a stimuli (Luck, 2005). ERP changes are reflective of increased EPSP prevalence (peak amplitude) or the rate of dipole fluctuations (peak latency) (Luck, 2005). There are numerous ERPs that can be predictably elicited across individuals. Response inhibition tasks, such as the modified Flanker task, reliably produce ERPs that can be used to compare intervention effects (Tillman & Wiens, 2011; Zurrón, Pouso, Lindín, Galdo, & Díaz, 2009). This study focused on the P300 ERP, described in more detail below.

4.2.1 P300 Waveform

The P300 waveform is an ERP that is elicited in decision-making (Donchin, 1981). Changes in P300 peak amplitude and latency are correlated with several aspects of cognitive

function including attentional capacity, response inhibition and working memory (Luck, 2005). The amplitude of this waveform is thought to be an indication of brain resource allocation for maintenance of working memory, response inhibition, and attention when a stimulus is presented. P300 latency is indicative of stimulus classification speed (Donchin, 1981).

The P300 consists of two subcomponents, the P3a and the P3b. The P3a is elicited by novel or uncommon target stimuli (Dien, Spencer, & Donchin, 2004; Polich, 2007). As an individual becomes more familiar with a task, the P3a becomes less prominent (Polich, 2007). The P3b is generated as a component of stimulus classification and plays a role in working memory (Polich, 2007). Repetitive tasks such as the modified Flanker task may elicit a visible P3a initially (primarily in practice trials in this study) and a P3b for both incongruent and congruent trials. The P3b will be the primary ERP of interest for this study.

5. Study Rationale

Previous research has suggested that cognitive function, specifically executive function and attention, is enhanced following an acute exercise session (Chang et al., 2012). High-intensity interval training (HIIT) is increasingly considered an efficient and possibly more effective strategy to improve cardiovascular health and metabolic control (Gibala et al., 2012). It may also improve cognitive function acutely after a single session; however, the influence of HIIT on cognitive function is poorly understood. While high intensity exercise has been demonstrated to have a negative impact on cognitive function during exercise, its effects post-exercise are variable and might be related to the timing post-exercise (Kamijo et al., 2007; Schmit et al., 2015). Specifically, it is possible that the cognitive benefits to HIIT occur after a short recovery period.

This study will compare the cognitive effects following an acute bout of HIIT and MCT to probe the influence of exercise intensity on cognitive function. Furthermore, cognitive function will be assessed over 45 minutes post-exercise in order to better understand the timing and duration of exercise-induced cognitive change by exercise intensity. Exploratory analyses will also consider whether the fitness of individuals alters the relative benefit of HIIT versus MCT and the timeline of cognitive changes. Significant results from this study will assist in determining optimal exercise prescription for an individual in order to enhance executive function and may provide insight into how exercise intensity alters cognitive changes.

6. Objectives and Hypotheses

1. To compare the changes in executive function (through behavioural and electrophysiological changes) immediately after HIIT, MCT, and rest, as measured using a modified Flanker task.

    1a. Relative to a rest session, cognitive function (as measured by behavioural and electrophysiological changes) will decrease immediately after the HIIT session (decreased P300 amplitude and increased P300 latency).

    1b. Relative to a rest session, cognitive function will improve immediately after a MCT session (increased P300 amplitude and decreased P300 latency).

    1c. Relative to MCT, cognitive function will be worse immediately after HIIT (P300 amplitude will be lower and P300 latency will be greater).

2. To compare the timing of cognitive changes after HIIT, MCT, and rest at four time points post-exercise: immediately post-exercise, 15 minutes, 30 minutes, and 45 minutes post-intervention.

    2a. Relative to a rest session, cognitive function will decrease immediately after HIIT; however, when measured after a delay post-exercise (15 minutes or more), cognitive

performance will improve and remain augmented (increased P300 amplitude and decreased P300 latency) for the duration recorded (45 minutes) but will display a trend towards baseline values by the final time point.

2b. Relative to a rest session, cognitive function will improve after the MCT session (increased P300 amplitude and decreased P300 latency) when measured immediately after exercise but will return to baseline levels by 45-minutes post-exercise.

2c. Relative to MCT, cognitive function immediately after exercise will be worse after HIIT (lower P300 amplitude and greater P300 latency). HIIT will reach the similar peak post-exercise values but the peak will occur after a delay rather than immediately post-exercise.

3. EXPLORATORY: To examine the influence of cardiorespiratory fitness on the cognitive response to acute sessions of HIIT and MCT.

3a. Higher fit individuals will not experience a negative cognitive response immediately after HIIT (no change in P300 amplitude or P300 latency from pre-values).

3b. Lower fit individuals will experience a decrease in cognitive performance (decreased P300 amplitude and increased P300 latency) immediately after HIIT before improving after a delay post-exercise (increased P300 amplitude and decreased P300 latency).

3c. Lower fit individuals will experience an increase in cognitive performance (increased P300 amplitude and decreased P300 latency) immediately after MCT before returning to baseline values by the last recorded time point (45 minutes post-exercise).

7. Methods

7.1 Participants

Twenty-two young, healthy participants were recruited from the University of Waterloo and the surrounding community (10 females; age = 23.5 ± 3.5 years). The full list of inclusion and exclusion criteria are detailed in Appendix A. Recruitment was performed through word of mouth and recruitment posters (see Appendix B). In brief, participants were screened as safe with no contraindications for exercise (using the Physical Activity Readiness Questionnaire (PAR-Q+, Appendix C)).

7.2 Sample Size

Sample size was based on detecting differences between each exercise session and the rest session. Based on prior literature, it was reasonable to predict a smaller effect size for HIIT (Chang et. al 2012); as such, sample size was based on these effects. In a recent meta-analysis of the acute effects of exercise on cognitive function, very hard exercise had an effect size of 0.465 for improved cognitive performance when measured after a delay of 1 minute or more after exercise (Chang et. al 2012). This is similar to the effect size for ERP measures (0.410) in a prior study (Kamijo et al., 2007). To estimate an effect size for this study, these two effect sizes were averaged for an effect size of 0.438. Based on an effect size of 0.438, an alpha level of 0.05, and a beta level of 0.8 in a repeated measures design, the estimated sample size required was 20 people. In order to allow for 10% loss of data (drop out or problems with data), 22 participants were planned for this study.

7.3 Study Design

This study used a repeated measures design and consisted of three sessions: 1) a

baseline/rest session; 2) a HIIT session; and 3) a MCT session. The order of the two exercise sessions (HIIT, MCT) was randomized. In each session, cognitive assessments were performed prior to the intervention (rest/MCT/HIIT) and at four time points after the intervention (immediately/0, 15, 30, 45 minutes). Sessions were scheduled 2 weeks apart to reduce practice effects but at the same time of day to control for circadian rhythm effects. Participants were asked to refrain from caffeine and exercise prior to testing on the day of their sessions. All three sessions took place in Lab 1015, Burt Matthews Hall.

7.3.1 Baseline/Rest Session

The baseline session was approximately three hours in length. This session started with the participant completing the PAR-Q+ (Appendix C) and the information consent form (Appendix D). The PAR-Q+ was used to screen whether it was safe for the participant to be involved in physical activity. Those who were confirmed to be eligible for the study then completed the International Physical Activity Questionnaire (IPAQ) (Appendix E) to assess habitual physical activity and provided demographic data (age, sex, education). Participants then had their height, weight, and resting heart rate measured.

After baseline screening and questionnaires, the participant completed the testing for the rest session. First, participants were fitted with a Polar H1 heart rate sensor and the Polar RS400 watch to monitor heart rate throughout the session. Second, the EEG cap was set up (details in section 7.5). Participants then performed 32 practice trials of the Flanker task. If they were comfortable with the task, they proceeded to testing. Otherwise, they performed another practice block of 32 trials. The pre-exercise trial consisted of one block of 200 trials of the Flanker task. (See section 7.4.2 for further description of the Flanker task.) The participant then performed one block of 200 trials of the Flanker Task immediately after, and 15, 30, and 45 minutes after 28.5

minutes of rest on a recumbent cycle ergometer. EEG was recorded concurrently with the Flanker task in order to generate ERPs time-locked to the task.

After the cognitive testing was complete, the EEG cap was removed. Participants then completed an incremental exercise step test in order to characterize aerobic fitness (VO_2peak) and to the prescription of exercise intensity in the subsequent sessions. (See section 7.4.1 for a detailed description of the exercise step test.)

7.3.2 High-Intensity Interval Training Session

Participants were fitted with a Polar H1 heart rate sensor and the Polar RS400 watch to monitor heart rate throughout the session. EEG and cognitive assessments were as described for the rest session. The exercise bout consisted of 3 minutes of warm-up at 30 Watts, 22.5min of HIIT, and 3 minutes of cool down at 30 Watts (28.5min total). The HIIT consisted of ten 60s intervals of high-intensity cycling on a recumbent cycling ergometer at a workload that corresponded to the maximal power achieved at the end of the exercise step test. These high intensity intervals were interspersed with periods of active rest consisting of 75s of cycling at a low intensity (30 Watts). Participants were required to maintain a cadence of 65rpm ± 5rpm throughout the exercise session. Participants were given feedback by the investigator if they needed to alter their cadence. If the participant was unable to maintain this cadence, then the workload was adjusted and recorded.

7.3.3 Moderate Intensity Continuous Training Session

The MCT session was identical to the HIIT session aside from the exercise performed. The MCT consisted of 3 minutes of warm-up at 30 Watts, 22.5min of continuous cycling on a recumbent ergometer for 22.5min, and 3 minutes of cool down at 30 Watts (28.5min total). Intensity corresponded with 85% of ventilatory threshold (VT). The MCT was designed to match

the HIIT session in Watt output.

7.4 Measures

7.4.1 Exercise Step Test

Peak oxygen uptake (VO_2peak) was determined through an exercise step test performed on a recumbent cycle ergometer. The participants performed a 3-minute warm-up at a predetermined load (50 W for men, 30 W for women) then proceeded to the test. The load was increased by a predetermined amount (30 W for men, 15 W for women) every minute until volitional fatigue (Hood, Little, Tarnopolsky, Myslik, & Gibala, 2011; Kamijo et al., 2004; Kamijo et al., 2007). The test was stopped when the participant met the criteria for VO_2peak or if the participant chose to at any time. VO_2peak criteria included one or more of the following: 1) a plateau in oxygen consumption, 2) heart rate failed to rise with increased exercise intensity (American College of Sports Medicine, 2013). If the participant chose to stop for a reason other than meeting VO_2peak criteria, the reason for stopping was recorded.

Gas exchange was measured throughout the exercise step test using a Cosmed K4b2 metabolic system. VO_2peak was calculated as the highest rate of oxygen consumption over a 10-breath average. Heart rate was continuously measured using a Polar H1 heart rate sensor beat by beat during this test. The subject's rating of perceived exertion was recorded every 2 minutes as an indication of perceived fatigue.

7.4.2 Eriksen Flanker Task

Executive function was assessed using the Eriksen Flanker Task (Eriksen and Eriksen, 1974) with concurrent EEG. This task is considered to be a measure of response inhibition, a component of executive function, as well as attention and information processing. The Flanker

task was administered using Stim2 software (Neuroscan). Participants were instructed to focus on a fixation cross on a television screen. Five arrows would appear on the screen. Participants were instructed to focus on the direction of the centre (target) arrow and to ignore the surrounding (flanking/distractor) arrows. There were two conditions for this task, congruent and incongruent. For congruent trials, the target arrow pointed in the same direction as the distractor arrows (e.g., <<<<<). This condition assesses attention and information processing. For incongruent trials, the target arrow pointed in the opposite direction of the distractor arrows (e.g., >><>>). This task additionally requires inhibition. The conditions of the task were randomized with a congruent to incongruent ratio of 1:1. When the target arrow was pointing to the left (<) participants used their right index finger to press the left button on the response pad. When the target arrow was pointing to the right (>) participants used their right middle finger to press the right button on the response pad. Participants were given earplugs to reduce auditory noise during the task. Participants were seated 185cm away from a 40-inch computer monitor in a dark room. A response pad was placed on a stand on their right side. Stimuli were presented for 500ms. There was a response window of 1000ms and an inter-stimulus interval of 1500ms. Each block of 200 stimuli took approximately 5 minutes to complete. Participants were instructed to respond as quickly as possible while still trying to achieve a high level of accuracy.

Performance measures included accuracy (% correct), response time (RT), interference effect (Incongruent RT – Congruent RT) and intra-individual coefficient of variability in RTs (ICV= Intra-individual RT standard deviation/individual mean RT*100). Responses that were not registered by the response pad and responses that exceeded the window of 1000ms were considered incorrect.

7.5 Electroencephalography Recording

The EEG signal was recorded using a QuickCap (Compumedics Neuroscan, Charlotte, NC). EEG data was recorded from the Oz, Pz, P3, P4, Cz, C3, C4, Fz, F3, and F4 electrode sites, according to the International 10-20 system and was referenced to the electrodes placed at both mastoids (see Appendix F). Impedances at EEG electrode sites were kept below 5kΩ. To monitor eye movement and other artifacts, electrooculogram (EOG) electrodes were placed above and below the right eye and lateral to both the right and left eye. Mastoid electrode sites were chosen as electrically neutral sites for active electrodes to be referenced. Impedances at EOG sites was kept below 10kΩ and at mastoid sites was kept below 5kΩ.

Data was recorded at 500 Hz using the Neuroscan Curry Software (Compumedics Neuroscan, Charlotte, NC). Presentation of cognitive stimulus and stimulus response was marked during the Flanker task in order to generate ERPs for analysis.

7.6 Analysis

7.6.1 EEG Analysis

EEG data recorded at the Pz electrode was analyzed using the Neuroscan Curry Software v.7.0.10 (Compumedics Neuroscan, Charlotte, NC). The EEG signal was referenced to both mastoids and digitally filtered using a 0.5 Hz high pass filter and a 30 Hz low pass filter. Trials were epoched from 100ms prior to cognitive stimuli and 1000ms post-cognitive stimuli. The signal was then baseline corrected to the pre-stimulus interval.

To reduce the impact of the high number of blinks and ocular artifacts, a covariance reduction method was used where eye movement or blinks (±75mV) within trials were reduced using a regression of the covariance of the signal present in the EOG. Each epoch was then visually inspected for excessive noise. Epochs still contaminated by artifacts after the covariance

reduction were removed from analysis. Remaining epochs were averaged by condition (congruent and incongruent). The mean amplitudes and latencies of the P300 ERP were used for analysis. The P300 amplitude was identified as the most positive peak between 250-750ms after stimulus presentation, measured in microvolts (μV). P300 latency was defined as the time (ms) at which this maximal positive peak occurred.

7.6.2 Data Analysis

Statistical analysis was performed with SAS 9.4. Participant characteristics are presented as mean ± standard error or percent as appropriate. The distribution of each outcome measure was examined and assessed for normality through histograms and probability plots and for homogeneity of variances with Mauchly's sphericity test. Due to significant violations of sphericity, a mixed regression analysis was used instead of analysis of variance (ANOVA). Mixed regression analysis does not require homogeneity of variance and also has the advantage of allowing unbalanced data. Pre-intervention values were also compared for all outcomes. If there were no significant difference in pre-intervention values, absolute data used for analyses. If there were significant differences in pre-intervention values, data was normalized to pre-intervention values (e.g. (post/pre) x 100%-100) was used for analyses.

A mixed effects linear regression model with repeated measures was conducted for each outcome (response accuracy, response time, interference effect, ICV, ERP amplitude and ERP latency). Session (rest, HIIT, and MCT) and time (pre, immediate, 15, 30 and 45), and a session x time interaction were included as within-subject factors. To determine whether fitness modified the relationship between session and cognitive function, VO2peak was also included as a covariate (between-subject factor) in the exploratory analysis. Tukey's HSD and separate one-way mixed regression analyses were used to examine differences when main or interaction

effects were found in primary analyses. An alpha level of 0.05 was used for all analyses.

8. Results

8.1 Participant Characteristics

Twenty-two participants (10 females; mean age: 22.7±5.4yrs) were recruited for this study. However, three participants were excluded from analysis, two because they did not complete all sessions and one because of repeated interruptions in testing, leaving a sample size of 19. Participant characteristics are further detailed in Table 1.

Table 1: Participant characteristics (n=19), mean ± SE.

Characteristic	**Men (n=9)**	**Women (n=10)**
Age (yrs)	24.0 ± 1.2	21.3 ± 6.2
Resting Heart Rate (bpm)	65.8 ± 1.4	73.3 ± 1.8
VO_2peak (mL/min/Kg)	35.6 ± 2.5	33.6 ± 1.5
IPAQ score	4167.7 ± 763.0	3367.8 ± 775.3
Body Mass Index (kg/m^2)	24.8 ± 1.5	22.9 ± 0.9

8.2 Exercise Step Test

Of 19 participants, 18 participants met objective criteria for VO_2peak. One participant chose to stop before a plateau in either VO_2 or HR occurred. The mean VO_2peak was 35.6 (2.5) in men and 33.6 (1.5) in women (Table 1). Using normative data from upright cycling VO_2peak tests, the male mean VO_2peak of 35.6 would qualify them into the poor fitness category and the female mean VO_2peak of 33.6 would qualify them into the good fitness category (American

College of Sports Medicine, 2013). For the purpose of exploratory analysis regarding potential effect modification by fitness, participants were stratified into three groups based on VO_2peak. Lowest fit females (n=3) had a VO_2peak lower than 30mL/min/kg, moderately fit (n=2) ranged from 30-35mL/min/kg, and the highest fit females (n=5) had a VO_2peak higher than 35mL/min/kg. Lowest fit males (n=2) had a VO_2peak lower than 30mL/min/kg, moderately fit (n=4) ranged from 30-40mL/min/kg, and the highest fit males (n=3) had a VO_2peak higher than 40mL/min/kg.

8.3 Exercise Characteristics

Exercise characteristics by session are presented in Table 2. Only one participant was unable to maintain the required cadence. This occurred in the HIIT session. As such, the load for MCT session was also reduced to allow for equal total time spent exercising between the HIIT and MCT sessions. All participants were able to maintain the required cadence at the assigned load for the MCT session.

Baseline HR was not significantly different between sessions ($F(2,53)=1.03$, $p=0.36$). However, HR during the intervention ($F(2,53)=565.24$, $p<0.0001$), and immediately, 15 minutes, 30 minutes and 45 minutes after intervention ($F(2,53)=53.11$, $p<0.0001$; $F(2,53)=24.67$, $p<0.0001$; $F(2,53)=16.94$, $p<0.0001$; $F(2,53)=11.69$, $p<0.0001$) was significantly different between sessions. HR was significantly higher during and after the HIIT session compared to the MCT session, which was higher than the rest sessions ($p<0.016$). Both exercise load (Watts) and estimated VO2 (mL/min/kg) were significantly different between the MCT and HIIT session ($F(1,18)=328.58$, $p<0.0001$; $F(1,18)=192.53$, $p<0.0001$).

Table 2. Exercise Characteristics by session (n=19), mean ± SE

Characteristic	Rest	HIIT	MCT	p-value
Resting HR	69.2 ± 1.6	72.6 ± 1.7	71.2 ± 2.0	p=0.36
Intervention HR	69.6 ± 1.4	157.9 ± 2.5	124.1 ± 3.2	p<0.0001
Immediately Post HR	71.3 ± 1.5	105.9 ± 3.2	85.4 ± 2.7	p<0.0001
15min Post HR	70.8 ± 1.9	98.8 ± 3.5	80.6 ± 2.3	p<0.0001
30min Post HR	69.7 ± 1.8	89.8 ± 2.9	77.3 ± 2.1	p<0.0001
45min Post HR	69.6 ± 8.5	85.9 ± 2.8	76.4 ± 1.7	p<0.0001
Load (W)	–	221.8 ± 10.7	94.7 ± 5.0	p<0.0001

8.4 Behavioral Data

Seven of 19 participants did not press the response button hard enough for a response to record for some responses. The portion of responses recorded varied by participant, session, and time point (mean: 93%, range: 57% to 100%). Since it is impossible to determine the accuracy of these responses and since the portion varied across session, we did not include accuracy as an outcome for analyses. Response time was deemed to be sufficiently accurate since at least 57 responses were averaged for each time point.

8.4.1 Response Time

Response time analyses revealed a main effect of congruency, ($F(1,18)=189.40$, $p<0.0001$) with incongruent trials having a longer response time (mean=411.42ms ± standard error=1.86) than the congruent trials (375.14ms ± 1.86). Response times were analyzed separately for congruent and incongruent trials.

8.4.1.1 Incongruent Response Time

Pre-intervention incongruent response time varied by session ($F(2,18)=9.48$, $p=0.0015$) so normalized data were used. Analysis of the normalized data yielded a session by time interaction ($F(6,100)=3.21$, $p=0.0064$). Post-hoc analyses revealed an effect of time in the rest session ($F(3,17)=4.79$, $p=0.010$) but not in the MCT ($F(3,17)=0.47$, $p=0.71$) or HIIT sessions ($F(3,17)=2.48$, $p=0.10$). The decrease in response time relative to baseline following rest was greater 30 minutes (-6.23% ± 0.95) and 45 minutes (-6.23% ± 0.82) after rest than immediately after (-3.09% ± 0.83). There was no significant change in response time over post-intervention time points during the MCT or HIIT sessions. There were also no differences at individual time points by session ($p>0.079$).

There were no main effects of session ($F(2,34)=0.83$, $p=0.45$) or time ($F(3,54)=1.36$, $p=0.27$). Normalized incongruent response times by session and time are displayed in Figure 1. Absolute incongruent response times by session and time are displayed in Table 3.

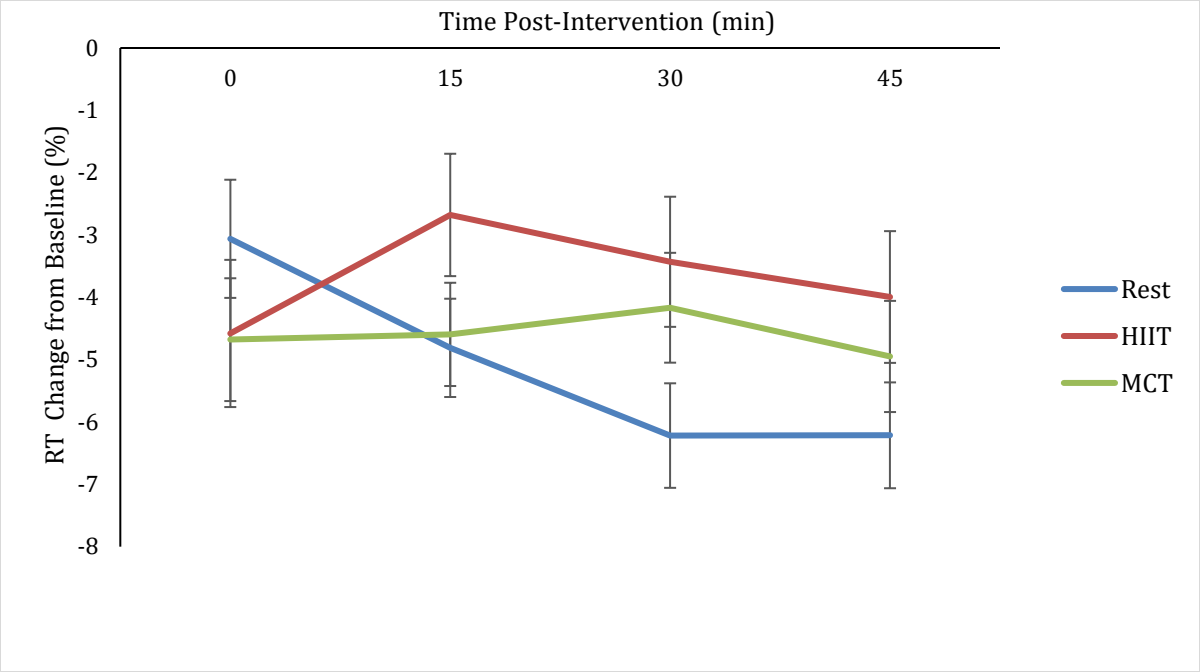

Figure 1. Mean normalized RT of correct incongruent trials of the modified Flanker Task by time and session. Each point represents mean change from pre (e.g. 15 min post/pre*100-100) ± standard error.

Table 3. RT (ms) for correct incongruent Flanker task trials by session and time (Mean ± SE).

Time	**Rest**	**HIIT**	**MCT**
Pre	444.2 ± 10.0	395.4 ± 15.7	417.6 ± 11.1
0 min	430.1 ± 5.8	392.6 ± 9.1	397.8 ± 6.4
15 min	422.7 ± 5.4	404.1 ± 8.5	398.1 ± 6.0
30 min	416.8 ± 5.7	401.2 ± 8.8	399.7 ± 6.3
45 min	416.6 ± 5.6	396.9 ± 8.6	396.6 ± 6.1

8.4.1.2 Congruent Response Time

Pre-intervention congruent response time varied by session ($F(2,18)=5.83$, $p=0.0112$) so normalized data were used. Analysis of normalized data indicated a main effect of time ($F(3,54)=3.20$, $p=0.030$). Post-hoc analysis of response times indicated that the decrease in response times (relative to pre-intervention) was greater immediately post-intervention (-3.28% ± 0.57) compared to 15 minutes after intervention (-2.03% ± 0.61).

The session by time interaction effect also neared statistical significance ($F(6,100)=2.10$, $p=0.060$). Exploratory post-hoc analysis revealed that there was a main effect of time in HIIT ($F(3,17)=3.68$, $p=0.036$) but not in the MCT ($F(3,17)=2.05$, $p=0.15$) or rest sessions ($F(3,17)=0.93$, $p=0.45$). The decrease in response time was greater immediately after HIIT (-3.37% ± 1.10) when compared to 15 minutes after HIIT (-1.02% ± 0.88). Furthermore, there were differences across sessions immediately post-intervention ($F(2,17)=5.09$, $p=0.019$) but not at other time points ($p>0.32$). Follow up indicated that the difference between MCT and rest neared significance ($p=0.073$), where there was a greater decrease in response times immediately after MCT (-4.34% ± 1.02) than immediately after rest (-1.93% ± 0.73).

There was no main effect of session ($F(2,34)=0.46$, $p=0.63$). Normalized congruent response times are displayed in Figure 2. Absolute congruent response times by session and time are displayed in Table 4.

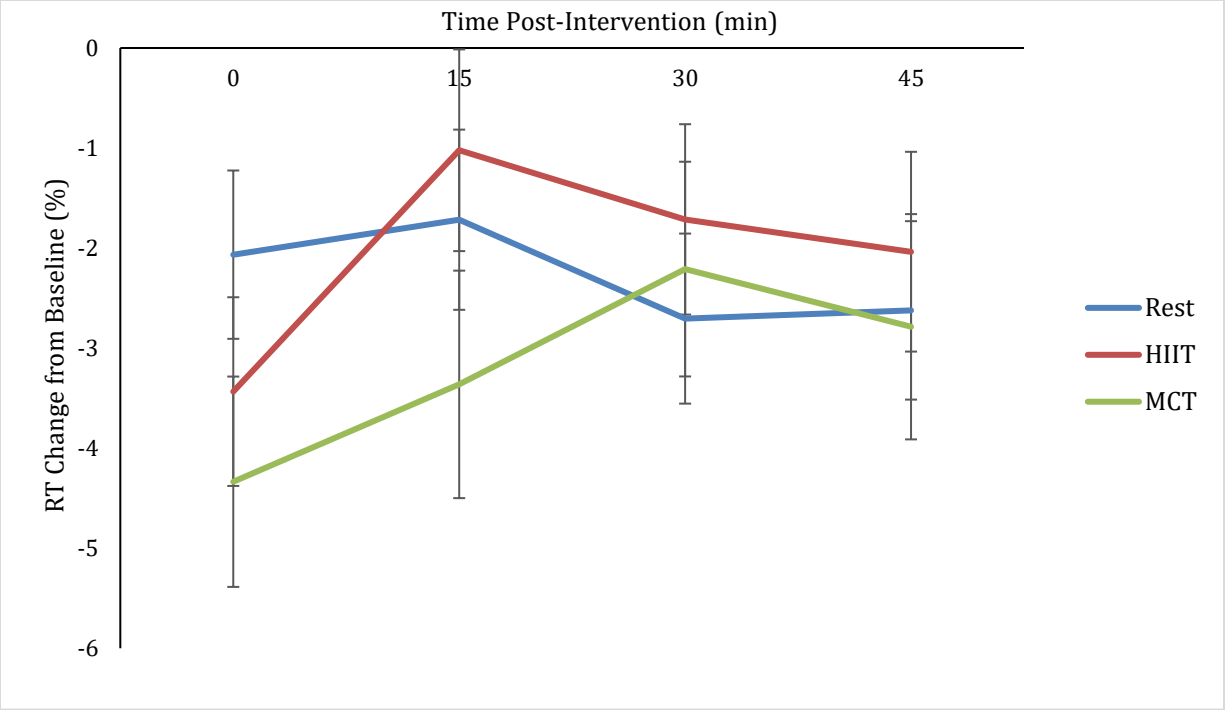

Figure 2. Mean normalized RT of correct congruent trials of the modified Flanker Task by time and session. Each point represents mean change from pre (e.g. 15 min post/pre*100-100) ± standard error.

Table 4. RT (ms) for correct congruent Flanker task trials by session and time (Mean ± SE).

Time	Rest	HIIT	MCT
Pre	390.6 ± 5.5	378.0 ± 5.8	381.2 ± 6.6
0 min	382.3 ± 5.2	364.9 ± 5.5	364.2 ± 6.3
15 min	383.4 ± 5.2	373.3 ± 5.4	367.6 ± 6.2
30 min	380.0 ± 5.5	371.0 ± 5.7	372.1 ± 6.6
45 min	380.0 ± 5.2	368.6 ± 5.4	369.9 ± 6.2

8.4.2 Interference Effect

Pre-intervention interference effect varied by session ($F(2,17)=16.23$, $p<0.0001$) so data was normalized to baseline values. Analysis of normalized data indicated a near-significant main effect of time ($F(3,54)=2.75$, $p=0.051$). Post-hoc analysis indicated that the change from baseline immediately post-intervention (-0.37% ± 9.14) was near-significantly different from that observed 15 (-14.89% ± 6.14, $p=0.093$), 30 (-22.22% ± 4.40, $p=0.063$) and 45 (-23.51% ± 6.032, $p=0.052$) minutes post-intervention. There was no main effect of session ($F(2,34)=0.50$, $p=0.61$) and no session by time interaction effect ($F(8,100)=0.15$, $p=0.99$). Normalized interference effect times by session and time are displayed in Figure 3. Absolute interference effect times by session and time are displayed in Table 5.

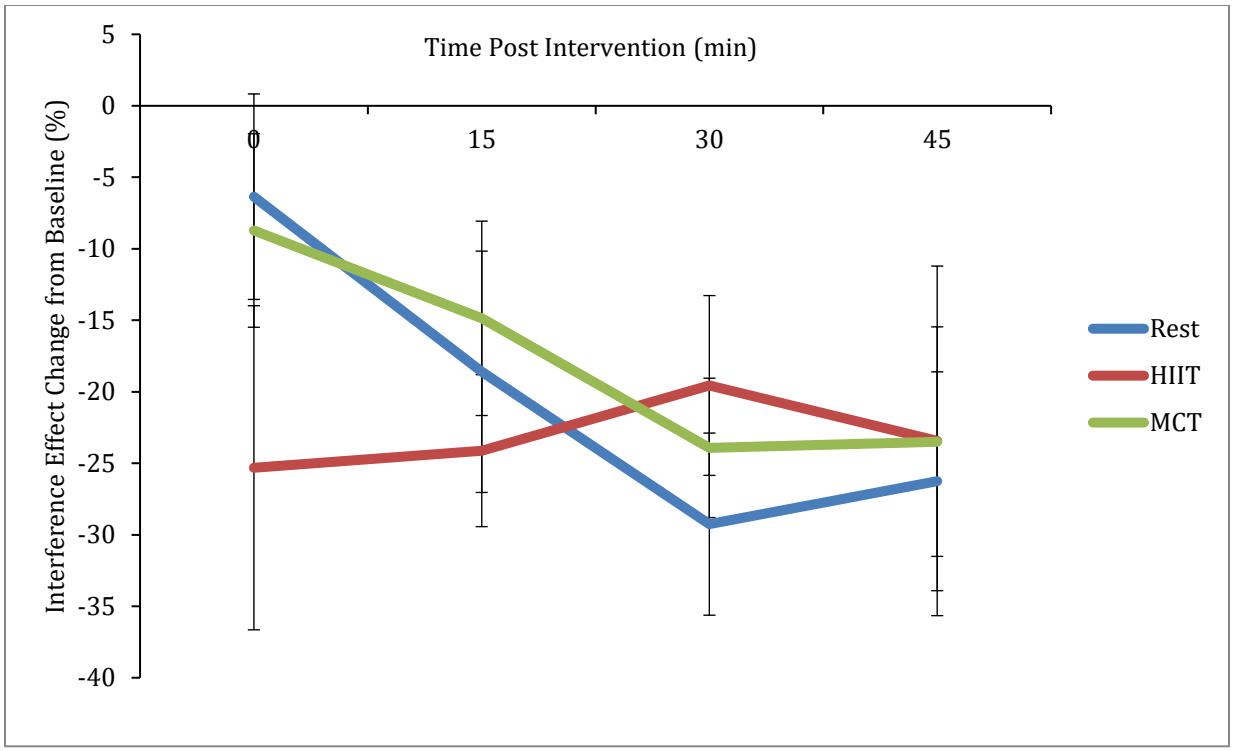

Figure 3. Mean normalized RT of correct congruent trials of the modified Flanker Task by time and session. Each point represents mean change from pre (e.g. 15 min post/pre*100-100) ± standard error.

Table 5. Interference effect (ms) for correct Flanker task trials by session and time (Mean ± SE).

Time	**Rest**	**HIIT**	**MCT**
Pre	53.6 ± 3.5	37.9 ± 3.1	36.4 ± 2.8
0 min	47.7 ± 3.8	31.7 ± 3.3	33.5 ± 3.0
15 min	39.3 ± 3.0	30.8 ± 2.7	30.5 ± 2.4
30 min	36.8 ± 3.5	30.2 ± 3.0	27.6 ± 2.8
45 min	36.6 ± 3.3	28.4 ± 2.9	26.7 ± 2.7

8.4.3 Intra-Individual Coefficient of Variation (ICV)

ICV analyses revealed a main effect of congruency ($F(1,17)=39.47$, $p<0.0001$) with incongruent trials having a higher ICV (12.66 ± 0.14) than congruent trials (12.66 ± 0.14). Incongruent and congruent ICV scores were analyzed separately.

8.4.3.1 Incongruent ICV

Analysis of the pre-intervention incongruent ICVs yielded a main effect of session ($F(2,18)=4.72$, $p=0.022$) so normalized data was used. There was no significant effect of session ($F(2,34)=2.45$, $p=0.10$) or time ($F(4,54)=0.57$, $p=0.63$) and no significant interaction between session and time ($F(6,100)=0.51$, $p=0.80$). Normalized incongruent ICV scores by session and time are displayed in Figure 4.

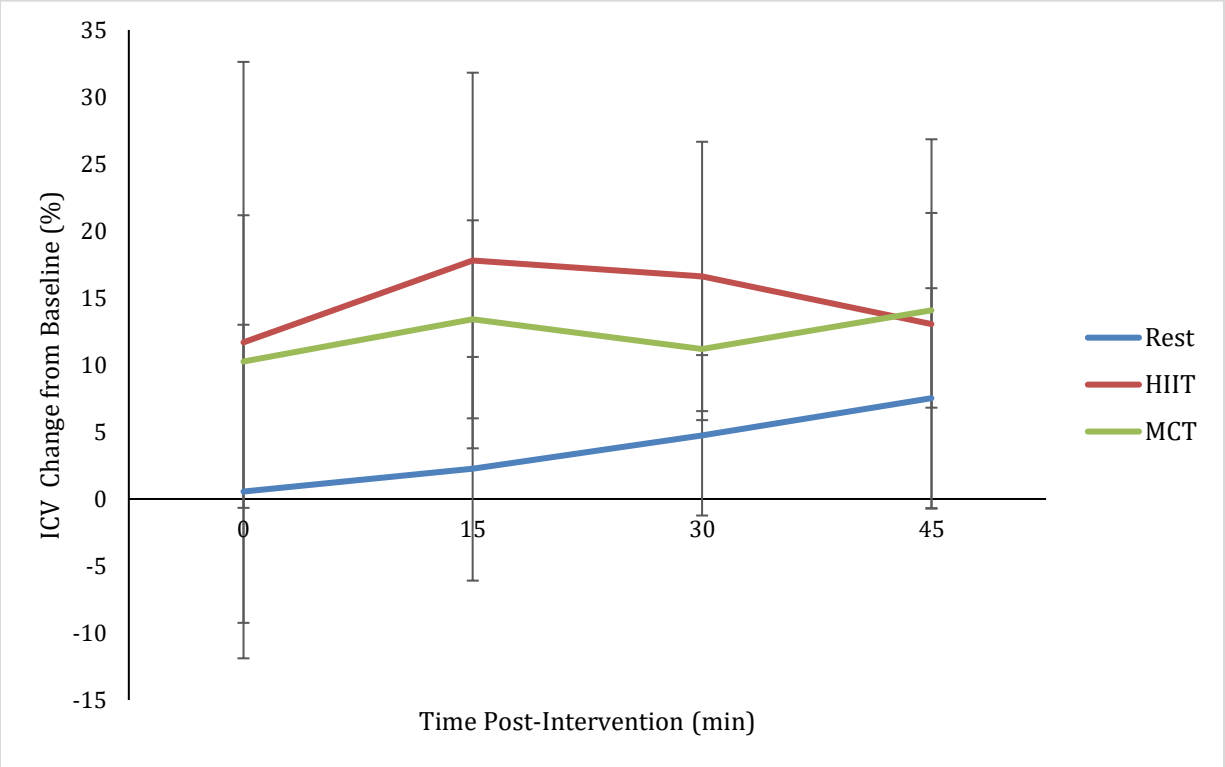

Figure 4. Mean normalized ICV score (SD/Mean RT*100) of correct incongruent trials of the modified Flanker Task by time and session. Each point represents mean change from pre (e.g. 15min post/pre*100-100) ± standard error.

8.3.3.2 Congruent ICV

Analysis of pre-intervention congruent ICV did not vary by session ($F(2,18)=0.21$, $p=0.81$) so absolute data was used. Analysis did not yield a main effect of time ($F(4,72)=0.98$, $p=0.42$) or session ($F(2,36)=0.00$, $p=0.99$) or a session by time interaction ($F(8,140)=1.14$, $p=0.34$). Absolute congruent ICV scores by session and time are displayed in Figure 5.

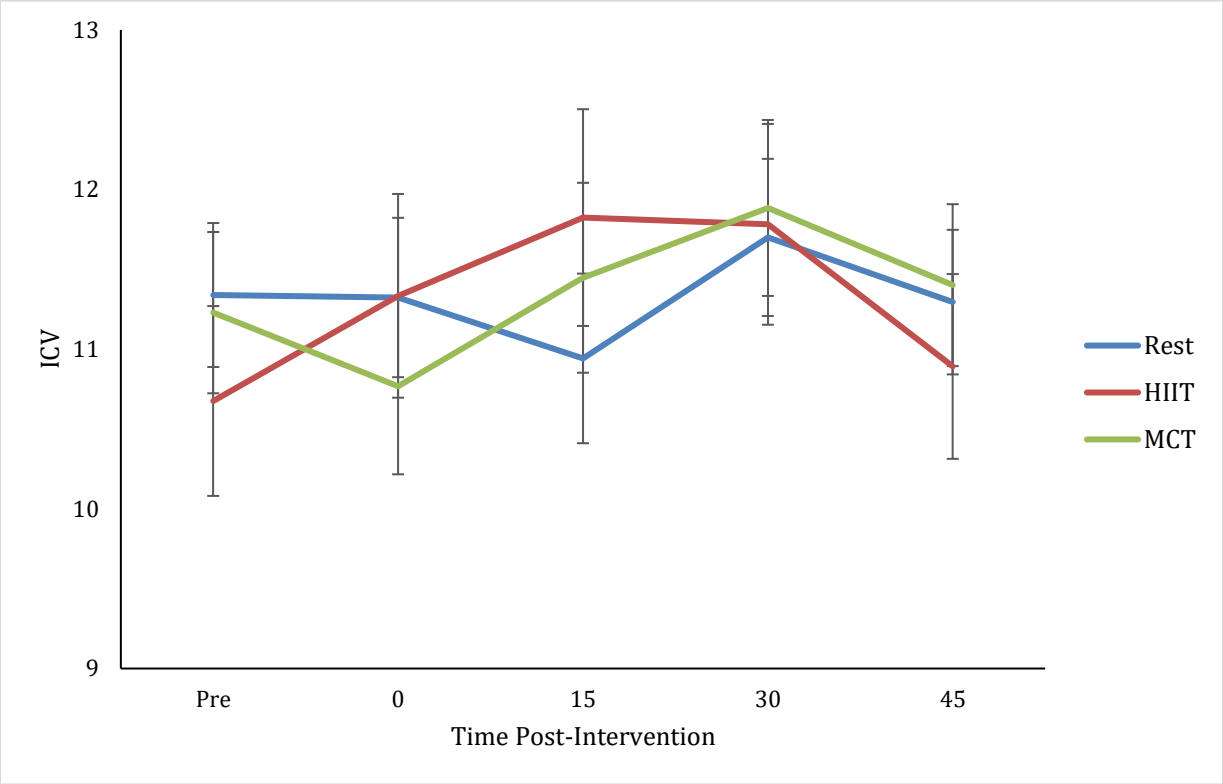

Figure 5. Mean ICV score (SD/Mean RT*100) of correct congruent trials of the modified Flanker Task by time and session. Each point represents mean ± standard error.

8.5 P300 Results

P300 amplitude and latency of correct, recorded trials were analyzed. The grand-average and individual waveforms immediately after the MCT session are displayed in Figure 6.

8.5.1 P300 Amplitude

There was not a significant main effect of congruency on P300 amplitude, though a trend was evident ($F(1,17)=3.06$, $p=0.081$). Incongruent and congruent P300 amplitude data were analyzed separately based on a priori hypotheses.

8.5.1.1 Incongruent P300 Amplitude

Analysis of pre-intervention absolute data did not reveal a main effect of session ($F(2,18)=0.96$, $p=0.40$) so absolute data was used. There was a significant main effect of time ($F(4,76)=2.49$, $p=0.050$). Post-hoc analyses revealed a trend towards greater P300 amplitude immediately after exercise ($9.64\mu V \pm 0.64$) when compared to 15 minutes after exercise ($9.02\mu V \pm 0.60$)($p=0.051$). There were no other differences by time. Analyses also yielded a significant session by time interaction ($F(8,148)=2.09$, $p=0.040$). Post-hoc analyses revealed a main effect of time in the MCT session ($F(4,17)=11.72$, $p<0.0001$) but not in the rest ($F(4,17)=0.54$, $p=0.71$) or HIIT sessions ($F(4,17)=2.57$, $p=0.076$). P300 amplitude was significantly higher immediately after MCT ($10.10\mu V \pm 0.89$) compared to 15 minutes ($9.05\mu V \pm 0.75$) and 45 minutes ($8.70\mu V \pm 0.75$) after MCT. None of the post-MCT time points were significantly different from pre-MCT score ($9.58\ \mu V \pm 0.78$) ($p>0.36$). Though the effect of time in the HIIT session neared significance, there were no differences in P300 amplitude by time within the session ($p>0.15$). There were also no differences across time points by session ($p>0.087$).

There was no main effect of session ($F(8,148)=0.55$, $p=0.58$). Incongruent P300 amplitude by time and session is displayed in Table 6 and Figure 7.

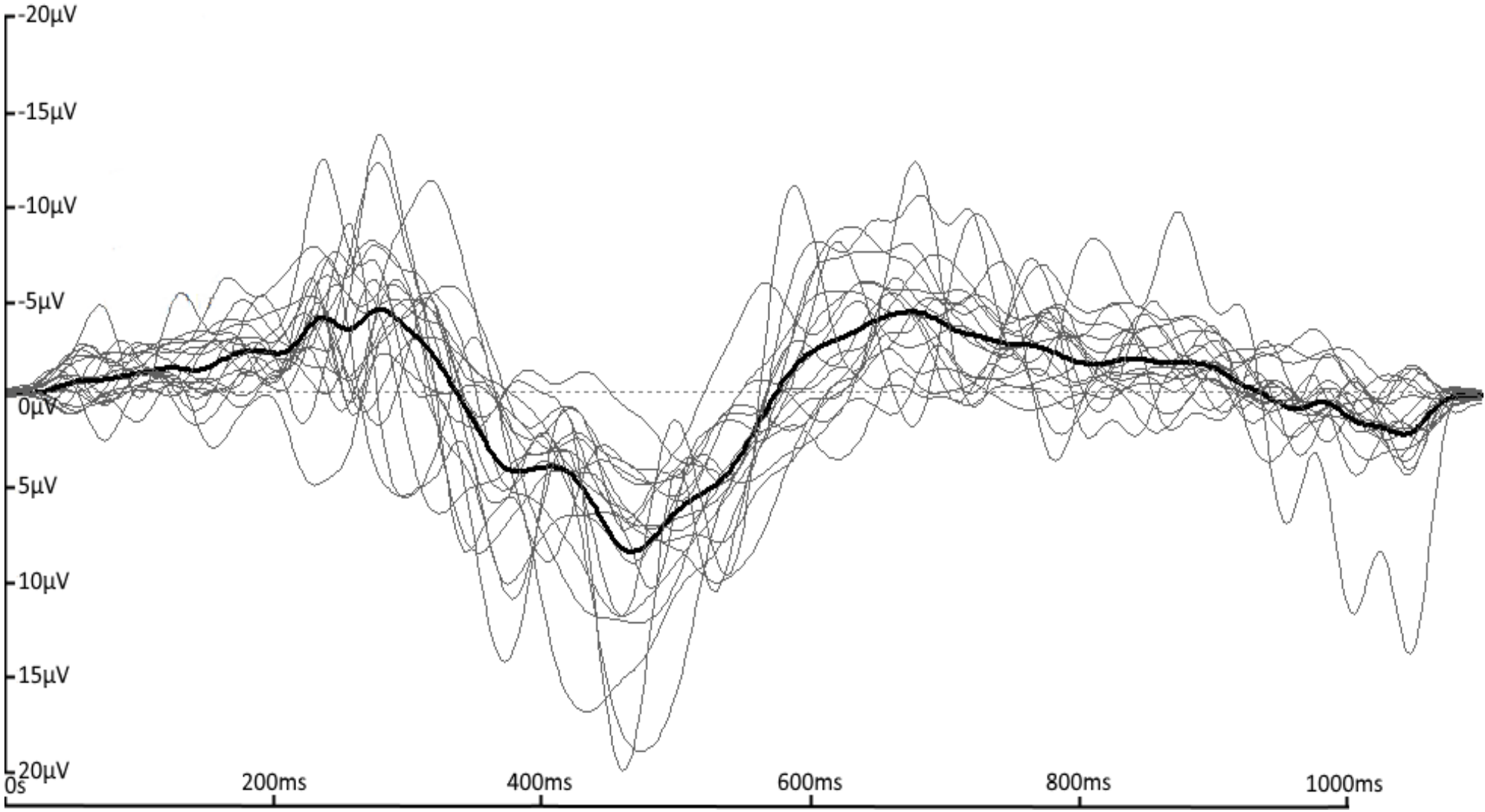

Figure 6. Grand averaged (bold, black line) and individual average tracings recorded at electrode Pz immediately after MCT for correct, congruent trials of the modified Flanker task.

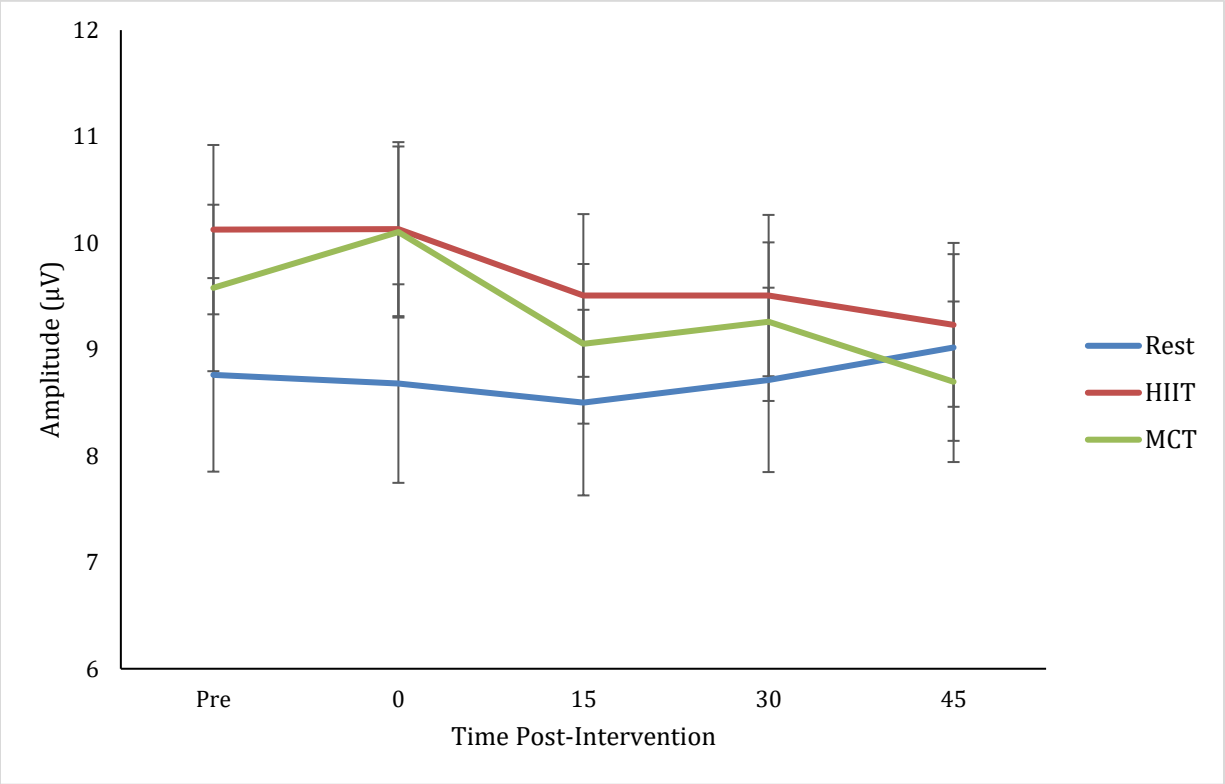

Figure 7. P300 amplitude (µV) on correct, incongruent trials of the modified Flanker task by time and session. Each point represents mean ± standard error.

Table 6. P300 amplitude (µV) on correct incongruent trials of the modified Flanker task trials by session and time (Mean ± SE).

Time	**Rest**	**HIIT**	**MCT**
Pre	8.8 ± 0.9	10.1 ± 0.8	9.6 ± 0.8
0 min	8.7 ± 0.9	10.1 ± 0.8	10.1 ± 0.8
15 min	8.5 ± 0.9	9.5 ± 0.8	9.1 ± 0.8
0 min	8.7 ± 0.9	9.5 ± 0.8	9.3 ± 0.7
45 min	9.0 ± 0.9	9.6 ± 0.8	8.7 ± 0.8

8.5.1.2 Congruent P300 Amplitude

Pre-intervention congruent P300 amplitude did not vary by session ($F(2,18)=0.16$, $p=0.85$) so absolute data was used. Analysis of the absolute data yielded a significant session by time interaction ($F(8,148)=3.45$, $p=0.0011$). Post-hoc analyses revealed a main effect of time in the MCT session ($F(4,17)=4.54$, $p=0.011$) but not in the rest ($F(4,17)=0.66$, $p=0.63$) or HIIT ($F(4,17)=1.57$, $p=0.23$) sessions. P300 amplitude was significantly higher both immediately after MCT ($10.23\mu V \pm 0.77$, $p=0.011$) and 15 minutes after MCT ($10.02\mu V \pm 0.77$, $p=0.041$) when compared to 45 minutes ($9.27\mu V \pm 0.77$) after MCT. None of the post-MCT time points were significantly different from pre-MCT score ($9.77\ \mu V \pm 0.75$) ($p>0.63$). Additional post-hoc analyses yielded a main effect of session immediately ($F(2,17)=5.61$, $p=0.014$) and at 30 minutes ($F(2,17)=4.54$, $p=0.026$) after intervention but not at other time points ($p>0.16$). P300 amplitude was significantly higher immediately after MCT ($10.23\mu V \pm 0.77$) compared to immediately after HIIT ($9.77\mu V \pm 0.76$). There was no difference in P300 amplitude immediately after MCT or HIIT and rest. At 30min post-intervention, P300 amplitude was significantly higher after MCT ($9.77\mu V \pm 0.80$) than after HIIT ($9.68\mu V \pm 0.79$). There was no difference at 30min post-intervention between MCT or HIIT and rest.

There was no main effect of either time ($F(4,76)=0.32$, $p=0.86$) or session ($F(8,148)=0.00$, $p=0.99$) on congruent P300 amplitude. Congruent P300 amplitude by session and time displayed in Table 7 and Figure 8.

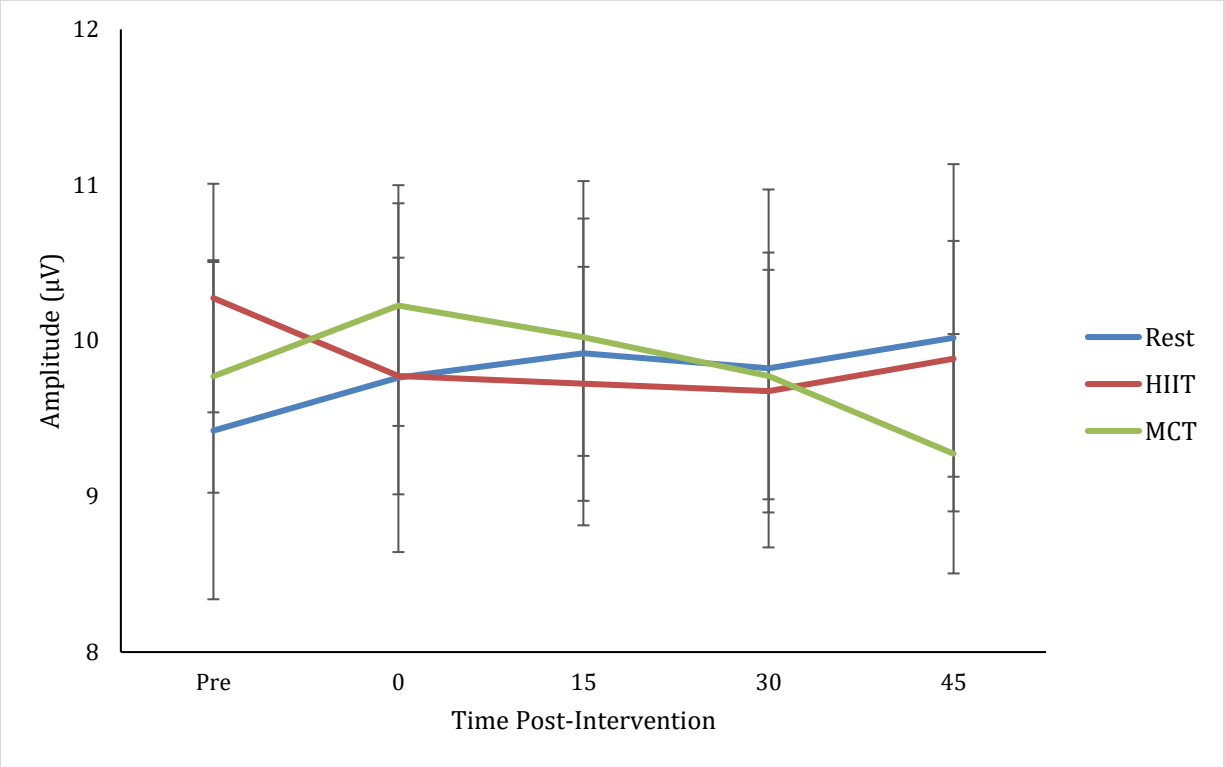

Figure 8. P300 amplitude (µV) on correct, congruent trials of the modified Flanker task by time and session. Each point represents mean ± standard error.

Table 7. P300 amplitude (µV) on correct, congruent trials of the modified Flanker task trials by session and time (Mean ± SE).

Time	**Rest**	**HIIT**	**MCT**
Pre	9.4 ± 1.1	10.3 ± 0.7	9.8 ± 0.7
0 min	9.8 ± 1.1	9.8 ± 0.8	10.2 ± 0.8
15 min	9.9 ± 1.1	9.7 ± 0.8	10.0 ± 0.8
30 min	9.8 ± 1.1	9.7 ± 0.8	9.8 ± 0.8
45 min	10.0 ± 1.1	9.9 ± 0.8	9.3 ± 0.8

8.5.2 P300 Latency

P300 Latency analyses revealed a main effect of congruency ($F(1,18)=74.01$, $p<0.0001$) with incongruent trials having a slower P300 latency (409.76ms ± 57.88) than the congruent trials (365.94ms ± 70.54). Incongruent and congruent trials were analyzed separately.

8.5.2.1 Incongruent P300 Latency

Pre-intervention congruent response time did not vary by session ($F(2,18)=1.23$, $p=0.32$) so absolute data was used. There was no significant main effect of time ($F(4,72)=2.37$, $p=0.060$) or session ($F(2,36)=0.70$, $p=0.50$) and no significant session by time interaction ($F(8,143)=0.33$, $p=0.95$). Incongruent P300 latency by time and session is displayed in Figure 9.

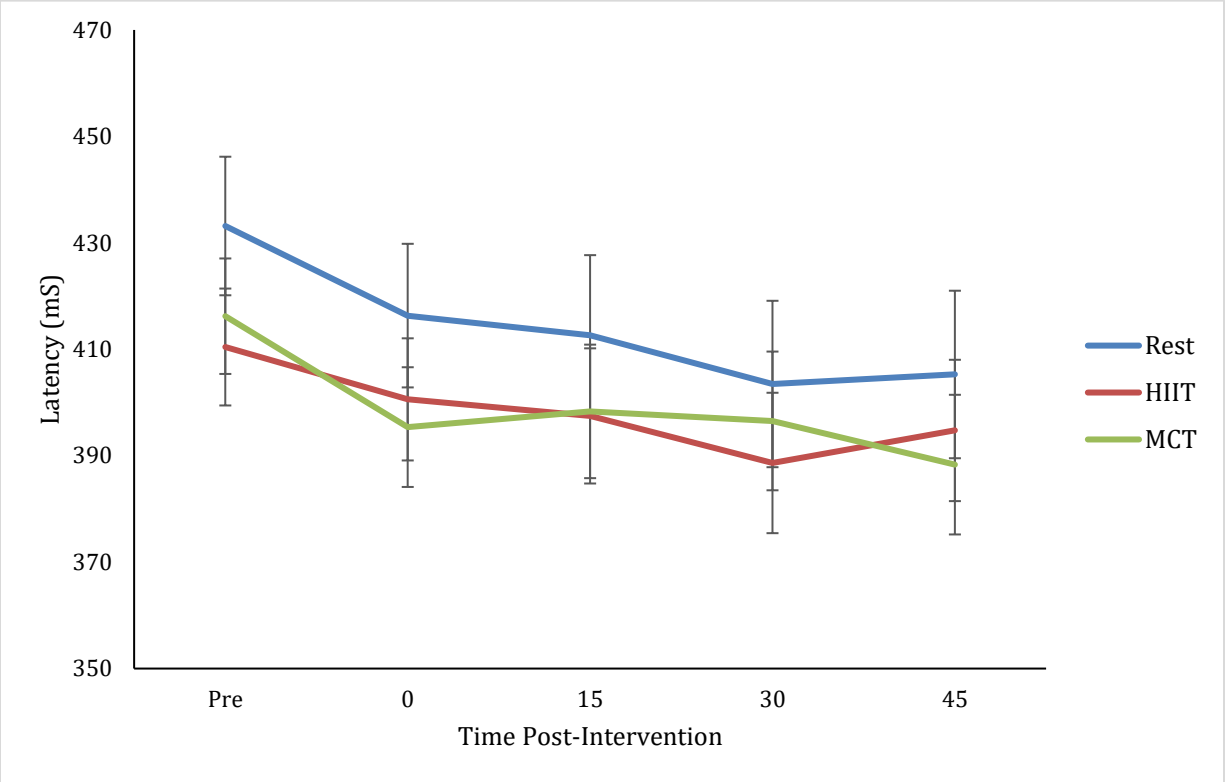

Figure 9. P300 Latency (ms) on correct, incongruent trials of the modified Flanker task by time and session. Each point represents mean ± standard error.

8.5.2.2 Congruent P300 Latency

Pre-intervention congruent response time did not vary by session ($F(2,18)=1.23$, $p=0.32$) so absolute data was used. There was no significant main effect of time ($F(4,72)=0.88$, $p=0.48$) or session ($F(2,36)=2.18$, $p=0.13$) and no significant session by time interaction ($F(8,143)=1.15$, $p=0.33$). Congruent P300 latency by time and session is displayed in Figure 10.

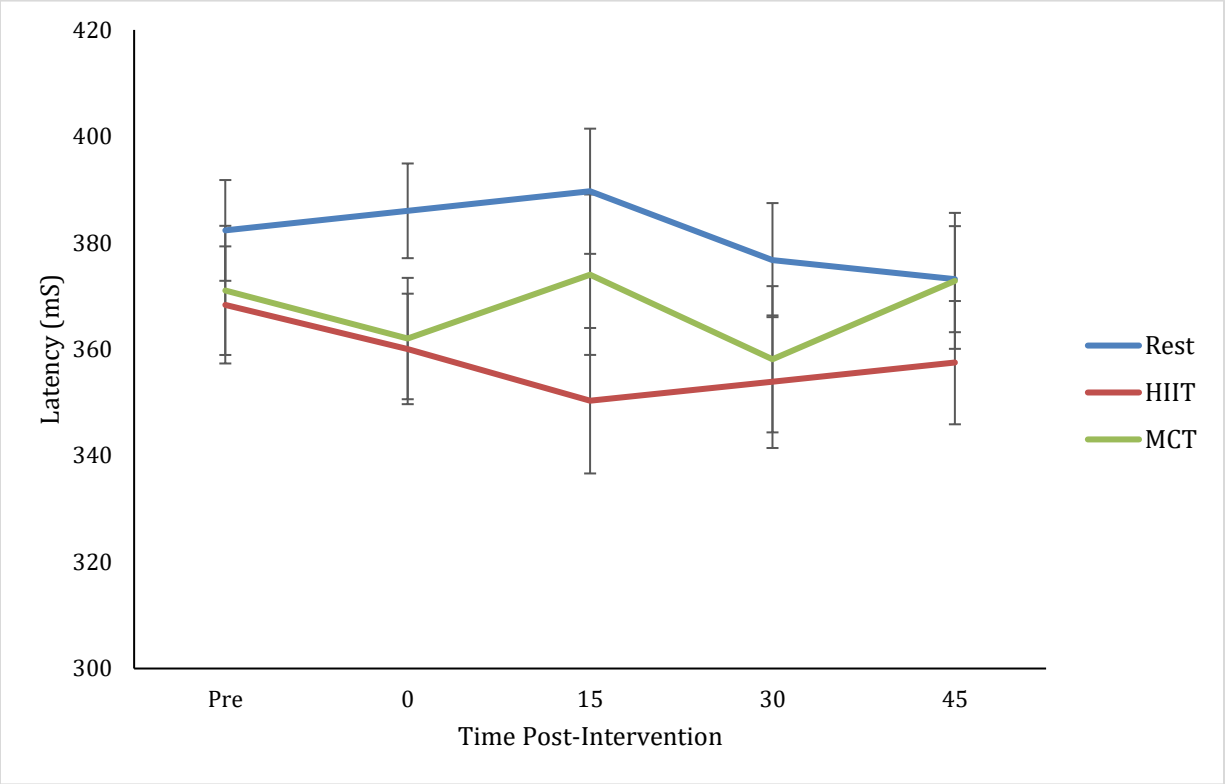

Figure 10. P300 Latency (ms) on correct, congruent trials of the modified Flanker task by time and session. Each point represents mean ± standard error.

8.6 Exploratory: Fitness as an Effect Modifier of Outcomes

8.6.1 Fitness as an Effect Modifier of Incongruent Response Time

Pre-intervention incongruent response time varied by session ($F(2,18)=9.48$, $p=0.0015$) so normalized data was used. When fitness group was included as a covariate in the model, there was no significant main effect of fitness ($F(2,16)=3.21$, $p=0.067$) or session by fitness interaction effect ($F(6,30)=0.95$, $p=0.48$) and no session by time by fitness interaction effect ($F(27,136)=1.40$, $p=0.11$).

8.6.2 Fitness as an Effect Modifier of Congruent Response Time

Pre-intervention congruent response time varied by session ($F(2,18)=5.83$, $p=0.0112$) so normalized data was used. When fitness group was included as a covariate in the model, there was no significant main effect of fitness ($F(2,16)=2.61$, $p=0.10$) or session by fitness interaction effect ($F(4,30)=1.13$, $p=0.36$) and no session by time by fitness interaction effect ($F(12,88)=1.40$, $p=0.40$).

9. Discussion

This study examined the effects of exercise intensity on response inhibition, information processing, and attention as assessed using a modified Flanker task and corresponding P300 waveforms. The results did not support the hypothesis that cognitive function improves following MCT and HIIT. Though there was some variability in cognitive function following MCT and HIIT, there were no significant differences between pre- and post-exercise cognitive function nor between exercise and the rest sessions. Though there were some differences between MCT and HIIT sessions, the results did not strongly support the hypothesis that cognitive function is variably effected by exercise intensity.

Based on existing literature, it was hypothesized that MCT would improve cognitive function immediately post-exercise but that cognitive function would return to pre-exercise performance by 45min post-exercise. The results of this study do not support this assertion. The improvement in response time observed after MCT was not significantly greater than that observed after rest, though it neared significance ($p=0.07$). Further, neither P300 amplitude nor P300 latency improved from pre- to post-MCT. The lack of significant cognitive benefits immediately after MCT is in contrast with most prior research and meta-analyses (Chang et al., 2012; Hillman et al., 2003; Joyce et al., 2014; Kamijo et al., 2004; 2007; Lambourne & Tomporowski, 2010; Yanagisawa et al., 2010), but not all (Joyce et al., 2009; Stroth et al., 2009). Despite the lack of significant cognitive improvements after MCT compared to rest, MCT did appear to have some influence on cognitive function. ERP measures of cognitive function varied over the 45min of testing post-MCT, though none were significantly different from the baseline values. P300 amplitude after MCT peaked immediately post-exercise and declined significantly by 45min post-exercise for both congruent and incongruent trials. The timeline for the drop in

P300 amplitude was more rapid for incongruent trials (where both 15min and 45min post were significantly lower than immediately post) than for congruent (where both immediately and 15min post were greater than 45min post). This evidence suggests that the effects of MCT are longer for attention and information processing (congruent trials) than for inhibition (incongruent trials).

Notably, the timeline for decline was similar to that observed in the few prior studies examining cognitive function over time post-exercise (Heckler & Croce, 1992; Joyce et al., 2014). Though results are somewhat variable across studies, cognitive effects were most frequently observed up to 15 minutes after exercise (Heckler & Croce, 1992; Joyce et al., 2014). In contrast, Joyce et al. (2009) found no improvement in cognitive function (inhibition) until 30 minutes after exercise.

Some previous studies suggest a greater exercise effect on response inhibition (incongruent trials) compared to attention or information processing (congruent trials) (Hillman et al., 2003; Kamijo et al., 2007). Notably, in prior studies, the differential effect by cognitive domain was only observed for P300 latency, but not for P300 amplitude or response time (Hillman et al., 2003; Kamijo et al., 2007). The differential effects by measure may be due to the inherent inaccuracy and variability associated with P300 latency measurement (Luck, 2005). The present study suggested few differences by congruency across measures, with only some suggestion that effects to P300 amplitude may last longer for congruent than incongruent trials. This is in line with some other studies and meta-analyses that similar benefits for inhibition and attention (Chang et al., 2012; Joyce et al., 2014). In particular, Joyce et al. (2014) examined the effect of acute exercise on performance on the Simon task and found a general decrease in RT and no specific influence on executive control.

In contrast to after MCT, it was hypothesized that there would be a decrease in cognitive function (as indicated by RT or P300 amplitude) immediately after HIIT but that cognitive function would improve relative to baseline by 15min after exercise. This was not observed. Similar to MCT, there was little evidence to suggest HIIT altered cognitive function relative to the rest session. There were no differences between the HIIT and rest sessions and there were no significant changes in cognitive function relative to pre-HIIT. Unlike MCT, P300 amplitude was not significantly higher immediately after HIIT relative to the subsequent time points, though visual inspection of results suggests a minor trend towards improvement in RT immediately post-HIIT followed by a return to baseline values 15 minutes post-HIIT. The lack of cognitive effects after HIIT is in line with some prior studies (Kamijo et al., 2004; 2007; Loprinzi & Kane, 2015), though not all (Budde et al., 2012; Hogervorst et al., 1996; Magnie et al., 2000). The reason for the contrasting results by study is unclear. It may be that high intensity exercise is more likely to elicit cognitive benefits after a delay, as evident in some studies and suggested by a meta-analysis (Chang et al., 2012; Magnie et al. 2000) but not immediately after exercise (Loprinzi & Kane, 2015; Kamijo et al., 2007). However, even though the current study included both immediate and delayed measures of cognitive function, no benefit to cognitive function was observed. It is possible that a combination of high fatigue and extended cognitive testing may have negated any delayed effects reported in past research (Magnie et al., 2000). The extended cognitive testing in the present study may have created a state of psychological fatigue, thereby decreasing the possibility to observe any delayed positive effects after exercise. This state of cognitive fatigue would be present across sessions but may have been interacted with the higher levels of physical fatigue found after HIIT to have more profound effects to cognitive function.

Fitness may have also confounded the cognitive effects of HIIT. One prior study found that only more fit individuals experienced cognitive benefits following high intensity exercise (Budde et al., 2013). Notably, this study defined the high fit group as individuals who performed at least 3 sessions of moderate or high intensity exercise per week so it is unclear whether activity levels or fitness may alter effects. In the present study, fitness was quantified using a VO_2peak test, the gold standard method, but we did not find differences in cognitive effects according to fitness level. Given the different methods of estimating fitness, it is difficult to compare the fitness of the current participants to the prior study. Any differences in fitness levels between samples may explain the inconsistent findings. Further, it is possible that the sample was too small in this study and underpowered to support the investigations by fitness, increasing the possibility of Type II error. As a result, the potential of effect modification by fitness and other factors should be explored further.

Although there were few significant cognitive benefits after exercise in this study, there is some evidence for differential effects by exercise intensity whereby MCT had a greater influence on cognitive function than HIIT. Borderline significant improvements on congruent RT were observed only for MCT. Furthermore, congruent P300 amplitude was significantly greater immediately and 30min after MCT relative to the HIIT session. This differential effect by exercise intensity has been observed previously (Kamijo et al., 2004; 2007; Loprinzi & Kane, 2015). The reason that HIIT may have fewer positive effects to cognitive function is unclear. It may be that HIIT induces more physiological and/or psychological stress, increasing cortisol and catecholamine release beyond the optimal point for cognitive functioning. After HIIT, participants may also experience more physical and psychological fatigue, which may reduce attention to the cognitive task (McMorris et al., 2016). In particular, the combined effects of

physical fatigue from HIIT with psychological fatigue from a high volume of cognitive testing may have negated any positive effects of exercise. It is possible that participants grew bored with the task, detrimentally affecting performance and, thereby, obscuring the cognitive effects over time. In the present study ICV scores provide some indication of this. There was a trend toward increasing at later time points. This trend denotes a potential decrease in cognitive function as a result of fatigue, though it would be difficult to separate the effects of fatigue from intervention effects.

Despite the variability in cognitive function post-exercise, especially post-MCT, the differences were not significantly different from pre-exercise or from the rest session. The lack of between session post-exercise differences was in contrast to a number of prior studies (Budde et al., 2013; Hillman et al., 2003; Joyce et al., 2009; 2014; Kamijo et al., 2004; 2007; Loprinzi & Kane, 2015), especially for MCT. There were a number of differences from prior studies that may account for the contrast in results, including the timing of assessments and the randomization of sessions. First, in contrast to most prior studies (Budde et al., 2013; Hillman et al., 2003; Joyce et al., 2009; 2014; Kamijo et al., 2004; 2007; Loprinzi & Kane, 2015), the rest session was always performed first rather than randomized or counter-balanced with the exercise sessions. As a result, it is likely that learning effects were concentrated in the rest session. It appeared that learning effects were further concentrated in the more difficult, incongruent condition, though a shorter learning effect may have occurred for congruent trials. Modified Flanker task response time during incongruent trials improved across all five time points in the rest session, suggesting a strong learning affect across the session. Furthermore, differences in incongruent versus congruent performance, as evidenced by ICV scores, was greater prior to the rest session compared to subsequent sessions, suggesting that learning effects may have carried

over to the exercise sessions. The learning effect in the rest session may have artificially inflated the pre- to post-rest differences, making it more difficult to detect differences with respect to pre- to post-exercise changes. Furthermore, learning carry-over may have inflated baseline cognitive performance pre-exercise relative to pre-rest.

Another disadvantage of the lack of randomization is that participants knew they were exercising in subsequent session. This knowledge may have induced activation of the stress response, releasing both cortisol and catecholamines due the perceived stress associated with upcoming exercise (Mason et al., 2003; McMorris et al., 2016). The activation of these systems may have improved cognitive processing pre-intervention, thereby reducing the likelihood of observing intervention effects. Indeed, heart rate was slightly higher in the MCT and especially the HIIT sessions compared to the rest session, though this difference was not significant. Unfortunately, heart rate was taken prior to EEG cap fitting, which may not best reflect the heart rate at cognitive testing or possible anticipatory effects.

Of note, the design of most prior studies would be able to separate anticipatory versus actual exercise effects. Most prior studies (Budde et al., 2013; Hillman et al., 2003; Joyce et al., 2009; 2014; Kamijo et al., 2004; 2007; Loprinzi & Kane, 2015), but not all (Del Giorno, Hall, O'Leary, Bixby, & Miller, 2010; Magnie et al., 2000), failed to include a pre-intervention cognitive assessment. As a result, it is difficult to determine whether the differences in cognitive function by session were present before exercise (which would reflect anticipatory effects), as in this study, or whether there was actually a pre- to post-exercise improvement. The augmentation of cognitive function pre-exercise in this study could have been due to several factors. The one prior study that included a pre-intervention assessment and found a significant improvement in ERP (P300, N400) after exercise kept participants naïve to the experimental procedure so

participants would not have had pre-exercise anticipatory arousal (Magnie et al., 2000). Unfortunately, this study did not include a rest session so differences in pre- to post-intervention change could not be compared to a rest control (Magnie et al., 2000). Comparing naïve participants to informed participants may be a way to characterize the influence of anticipatory arousal on observed exercise effects. Notably, a second study that included a pre-intervention cognitive assessment found no significant improvements in cognitive function after exercise (Del Giorno et al., 2010), though a trend towards improvement was evident.

9.1 Limitations

This study was the first to measure the influence of exercise intensity on cognitive performance for an extended duration post-intervention. However there are several limitations to this study. Most notably, the lack of randomization of the rest session likely reduced our ability to detect exercise effects. A learning effect was evident in the rest session, particularly for incongruent trials, increasing pre- to post-rest cognitive changes and thereby reducing our ability to detect a difference relative to pre- to post-exercise changes. Secondly, due to the lack of randomization of the rest session, participants were aware they would have to exercise in subsequent sessions, though the intensity was unknown until after pre-intervention measures were complete. The anticipatory arousal prior to the exercise sessions may have improved pre-exercise cognitive function and decreased the magnitude of pre- to post-exercise changes. There were also many sources of variability that could not be controlled. Though participants were instructed to avoid caffeine and exercise on the days of testing, we did not objectively confirm that they followed instructions or control for the amount of water or food consumed. Furthermore, each session was scheduled for the same time of day on the same day of the week

in order to ensure the participant's daily schedule would be minimally altered. However, this precaution did not account for any changes in stress the participant was experiencing day to day or week to week. Finally, though impedances were kept below 5kΩ, variability within that range was present. This may alter observed P300 waveforms.

Finally, this study relied on analysis of the P300 as an indication of electrophysiological changes after exercise. Due to the low spatial resolution of EEG, ERP analysis is limited in its ability to infer specific regions of brain activity associated with cognitive processes (Luck, 2005). Additionally, ERP analysis requires averaging across trials to reduce noise in order to obtain averaged peak values. The averaging process reduces the ability to explore within-subject variability of electrophysiological changes trial to trial. Within-subject variability remains a relatively unexplored topic of research that may provide insight into a cognitive response to exercise. Future research should consider alternative methods of EEG analysis to account for within subject variability. A particularly promising technique is single trial analysis of ERP data using an independent component analysis allows for the examination of ERP fluctuations on a trial to trial level and may be a valuable method for analyzing within-subject variability in future research (Ribeiro, Paiva, & Castelo-Branco, 2016).

9.2 Conclusion

HIIT remains a time efficient strategy to induce physiological adaptations; however, the present study suggests HIIT does not benefit cognitive function. In this study, neither MCT nor HIIT had acute benefits to response inhibition, information processing or attention, though some evidence of post-exercise variability in cognitive function was observed. This is in contrast to many prior studies, especially for MCT. The reason for a lack of effects is unclear but may be due to the inclusion of pre-intervention testing or the lack of randomization of the baseline

session. Anticipatory arousal pre-exercise may have reduced observed pre- to post-exercise changes. Furthermore, learning effects in the rest session may have reduced the contrast in pre- to post-intervention changes between the rest and exercise sessions. Future studies using the modified Flanker task should randomize all sessions or include extensive practice opportunities to control for the learning effects. Future studies should also evaluate the influence of anticipatory arousal on pre-exercise cognitive performance by randomizing participants to informed or naïve conditions.

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Appendices

Appendix A

Inclusion and Exclusion Criteria

Inclusion and Exclusion Criteria

Inclusion	**Exclusion**
• Healthy • 18-25 years old • Screened safe to exercise (PAR-Q)	• History of heart disease • Uncontrolled diabetes • Uncontrolled hypertension • Dramatic drop in blood pressure when you rise from a seated position (symptoms include dizziness and feeling like you will faint) • Neurological conditions including stroke, epilepsy, Parkinson's disease, or dementia • Are taking beta blockers, anticoagulants, or anticholinergics • Chronic obstructive pulmonary disease • Musculoskeletal impairments that cause more pain during exercise than is tolerable • History of allergies to electrode gel or adhesive • Injuries that cause excessive pain during exercise • Recent concussion or history of multiple concussions • Cardiorespiratory conditions that may prevent maximal exertion or wearing a mask during exercise

Appendix B

Recruitment Poster

Department of Kinesiology
University of Waterloo

PARTICIPANTS NEEDED FOR A RESEARCH STUDY:

The Effects of Exercise Intensity on Cognitive Function

We are looking for volunteers to take part in a study of the effect of *Exercise Intensity on Cognitive Function.* As a participant in this study, you would be asked to:

- Perform exercise on a stationary bicycle that will test your fitness and have your breathing measured during exercise.
- Perform basic tests of your memory, attention, and decision making ability and have your brain activity monitored during these tasks.
- Wear non-invasive equipment to measure brain and physical activity.
- Inform us of your normal physical activity levels.
- Perform a 25 minutes of moderate- to high-intensity exercise.

Your participation would involve *THREE* sessions, each about 2 weeks apart. The first session will be approximately 2.5 hours in length and the second and third will be approximately 2 hours.

You are ineligible for the study if you have medical conditions that could worsen with exercise, have unstable cardiovascular disease, or have any neurological condition such as epilepsy or stroke.

For more information or to volunteer for this study, please contact:

Spencer Wikkerink
swikkeri@uwaterloo.ca
519-888-4567 ext. 38548

This study has been reviewed by and received ethics clearance through a University of Waterloo Research Ethics Committee.

Appendix C

Physical Activity Readiness Questionnaire (PAR-Q+)

CSEP approved Sept 12 2011 version

PAR-Q+

The Physical Activity Readiness Questionnaire for Everyone

Regular physical activity is fun and healthy, and more people should become more physically active every day of the week. Being more physically active is very safe for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor OR a qualified exercise professional before becoming more physically active.

SECTION 1 - GENERAL HEALTH

Please read the 7 questions below carefully and answer each one honestly: check YES or NO.		YES	NO
1.	Has your doctor ever said that you have a heart condition OR high blood pressure?	☐	☐
2.	Do you feel pain in your chest at rest, during your daily activities of living, OR when you do physical activity?	☐	☐
3.	Do you lose balance because of dizziness OR have you lost consciousness in the last 12 months? Please answer NO if your dizziness was associated with over-breathing (including during vigorous exercise).	☐	☐
4.	Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)?	☐	☐
5.	Are you currently taking prescribed medications for a chronic medical condition?	☐	☐
6.	Do you have a bone or joint problem that could be made worse by becoming more physically active? Please answer NO if you had a joint problem in the past, but it does not limit your current ability to be physically active. For example, knee, ankle, shoulder or other.	☐	☐
7.	Has your doctor ever said that you should only do medically supervised physical activity?	☐	☐

If you answered NO to all of the questions above, you are cleared for physical activity.

Go to Section 3 to sign the form. You do not need to complete Section 2.

- Start becoming much more physically active – start slowly and build up gradually.
- Follow the Canadian Physical Activity Guidelines for your age (www.csep.ca/guidelines).
- You may take part in a health and fitness appraisal.
- If you have any further questions, contact a qualified exercise professional such as a CSEP Certified Exercise Physiologist® (CSEP-CEP) or CSEP Certified Personal Trainer® (CSEP-CPT).
- If you are over the age of 45 yrs. and NOT accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

If you answered YES to one or more of the questions above, please GO TO SECTION 2.

Delay becoming more active if:

- You are not feeling well because of a temporary illness such as a cold or fever – wait until you feel better
- You are pregnant – talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the PARmed-X for Pregnancy before becoming more physically active OR
- Your health changes – please answer the questions on Section 2 of this document and/or talk to your doctor or qualified exercise professional (CSEP-CEP or CSEP-CPT) before continuing with any physical activity programme.

SECTION 2 - CHRONIC MEDICAL CONDITIONS

	Please read the questions below carefully and answer each one honestly: check YES or NO.	YES	NO
1.	Do you have Arthritis, Osteoporosis, or Back Problems?	☐ If yes, answer questions 1a-1c	☐ If no, go to question 2
1a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
1b.	Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/or spondylolysis/pars defect (a crack in the bony ring on the back of the spinal column)?	☐	☐
1c.	Have you had steroid injections or taken steroid tablets regularly for more than 3 months?	☐	☐
2.	Do you have Cancer of any kind?	☐ If yes, answer questions 2a-2b	☐ If no, go to question 3
2a.	Does your cancer diagnosis include any of the following types: lung/bronchogenic, multiple myeloma (cancer of plasma cells), head, and neck?	☐	☐
2b.	Are you currently receiving cancer therapy (such as chemotherapy or radiotherapy)?	☐	☐
3.	Do you have Heart Disease or Cardiovascular Disease? This includes Coronary Artery Disease, High Blood Pressure, Heart Failure, Diagnosed Abnormality of Heart Rhythm	☐ If yes, answer questions 3a-3e	☐ If no, go to question 4
3a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
3b.	Do you have an irregular heart beat that requires medical management? (e.g. atrial fibrillation, premature ventricular contraction)	☐	☐
3c.	Do you have chronic heart failure?	☐	☐
3d.	Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer YES if you do not know your resting blood pressure)	☐	☐
3e.	Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?	☐	☐
4.	Do you have any Metabolic Conditions? This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes	☐ If yes, answer questions 4a-4c	☐ If no, go to question 5
4a.	Is your blood sugar often above 13.0 mmol/L? (Answer YES if you are not sure)	☐	☐
4b.	Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, and the sensation in your toes and feet?	☐	☐
4c.	Do you have other metabolic conditions (such as thyroid disorders, pregnancy-related diabetes, chronic kidney disease, liver problems)?	☐	☐
5.	Do you have any Mental Health Problems or Learning Difficulties? This includes Alzheimer's, Dementia, Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndrome)	☐ If yes, answer questions 5a-5b	☐ If no, go to question 6
5a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
5b.	Do you also have back problems affecting nerves or muscles?	☐	☐

			YES	NO
	Please read the questions below carefully and answer each one honestly: check YES or NO.			
6.	Do you have a Respiratory Disease? This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure		☐ If yes, answer questions 6a-6d	☐ If no, go to question 7
	6a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	6b.	Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen therapy?	☐	☐
	6c.	If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough (more than 2 days/week), or have you used your rescue medication more than twice in the last week?	☐	☐
	6d.	Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?	☐	☐
7.	Do you have a Spinal Cord Injury? This includes Tetraplegia and Paraplegia		☐ If yes, answer questions 7a-7c	☐ If no, go to question 8
	7a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	7b.	Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?	☐	☐
	7c.	Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?	☐	☐
8.	Have you had a Stroke? This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event		☐ If yes, answer questions 8a-c	☐ If no, go to question 9
	8a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer NO if you are not currently taking medications or other treatments)	☐	☐
	8b.	Do you have any impairment in walking or mobility?	☐	☐
	8c.	Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?	☐	☐
9.	Do you have any other medical condition not listed above or do you live with two chronic conditions?		☐ If yes, answer questions 9a-c	☐ If no, read the advice on page 4
	9a.	Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months OR have you had a diagnosed concussion within the last 12 months?	☐	☐
	9b.	Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?	☐	☐
	9c.	Do you currently live with two chronic conditions?	☐	☐

Please proceed to Page 4 for recommendations for your current medical condition and sign this document.

PAR-Q+

If you answered NO to all of the follow-up questions about your medical condition, you are ready to become more physically active:

- It is advised that you consult a qualified exercise professional (e.g., a CSEP-CEP or CSEP-CPT) to help you develop a safe and effective physical activity plan to meet your health needs.
- You are encouraged to start slowly and build up gradually – 20-60 min. of low- to moderate-intensity exercise, 3-5 days per week including aerobic and muscle strengthening exercises.
- As you progress, you should aim to accumulate 150 minutes or more of moderate-intensity physical activity per week.
- If you are over the age of 45 yrs. and NOT accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

If you answered YES to one or more of the follow-up questions about your medical condition:

- You should seek further information from a licensed health care professional before becoming more physically active or engaging in a fitness appraisal and/or visit a or qualified exercise professional (CSEP-CEP) for further information.

Delay becoming more active if:

- You are not feeling well because of a temporary illness such as a cold or fever – wait until you feel better
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise profesional, and/or complete the PARmed-X for Pregnancy before becoming more physically active OR
- Your health changes - please talk to your doctor or qualified exercise professional (CSEP-CEP) before continuing with any physical activity programme.

SECTION 3 - DECLARATION

- You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.
- The Canadian Society for Exercise Physiology, the PAR-Q+ Collaboration, and their agents assume no liability for persons who undertake physical activity. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.
- If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.
- Please read and sign the declaration below:

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that a Trustee (such as my employer, community/fitness centre, health care provider, or other designate) may retain a copy of this form for their records. In these instances, the Trustee will be required to adhere to local, national, and international guidelines regarding the storage of personal health information ensuring that they maintain the privacy of the information and do not misuse or wrongfully disclose such information.

NAME _____ DATE _____

SIGNATURE _____ WITNESS _____

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER _____

For more information, please contact:
Canadian Society for Exercise Physiology
www.csep.ca

KEY REFERENCES
1. Jamnik VJ, Warburton DER, Makarski J, McKenzie DC, Shephard RJ, Stone J, and Gledhill N. Enhancing the eectiveness of clearance for physical activity participation: background and overall process. APNM 36(S1):S3-S13, 2011.
2. Warburton DER, Gledhill N, Jamnik VK, Bredin SSD, McKenzie DC, Stone J, Charlesworth S, and Shephard RJ. Evidence-based risk assessment and recommendations for physical activity clearance: Consensus Document. APNM 36(S1):S266-s298, 2011.

The PAR-Q+ was created using the evidence-based AGREE process (1) by the PAR-Q+Collaboration chaired by Dr. Darren E. R. Warburton with Dr. Norman Gledhill, Dr. Veronica Jamnik, and Dr. Donald C. McKenzie (2). Production of this document has been made possible through financial contributions from the Public Health Agency of Canada and the BC Ministry of Health Services. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada or BC Ministry of Health Services.

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THE GOLD STANDARD IN EXERCISE SCIENCE AND PERSONAL TRAINING

CSEP approved Sept 12 2011 version

Appendix D

Information Consent Form

UNIVERSITY OF WATERLOO

INFORMATION CONSENT FORM

Physical Activity and Cognitive Function

Student Investigator
Spencer Wikkerink, BSc, University of Waterloo, Department of Kinesiology, swikkeri@uwaterloo.ca 519-888-4567 Ext. 38548

Faculty Supervisor
Laura Middleton, PhD, University of Waterloo, Department of Kinesiology, laura.middleton@uwaterloo.ca 519-888-4567 Ext. 33045

INTRODUCTION

You are being invited to take part in a research study that will form the basis of Spencer Wikkerink's Master's thesis. Before agreeing to participate in this study, it is important that you read the study procedures. The following information describes the purpose, procedures, benefits, discomforts, risks, and precautions associated with this study. It also describes your right to refuse to participate or withdraw from the study at any time. In order to decide whether you wish to participate in this research study, you should be aware of its risks and benefits to be able to make an informed decision. This is known as the informed consent process. Please ask the study staff to explain any details that are unclear before signing this consent form. Make sure all your questions have been answered to your satisfaction before signing this form.

WHAT IS THE PURPOSE OF THIS STUDY?

Physical activity is recommended as an important aspect of physical health. Growing research suggests that physical activity is not only associated with physical health but also thinking abilities. The purpose of this study is to determine how varying exercise intensity may affect your thinking abilities and brain health.

ELIGIBILITY

You are eligible for this study if you are a healthy young adult (18-35 years). You are ineligible if you have an unstable medical condition that could make exercise unsafe or have a condition that would interfere with the study procedures. These include:

- History of heart disease (heart attack or operation, heart murmur, coronary artery disease, congenital heart disease, pacemaker)
- Uncontrolled diabetes (your blood sugar levels are not well regulated by medicine, diet or exercise)

- Uncontrolled hypertension (your blood pressure is not well regulated with or without medicine)
- Drop in blood pressure when you rise from a seated position (symptoms include dizziness and feeling like you will faint)
- Neurological conditions including stroke, epilepsy, Parkinson's disease, or dementia
- Are taking beta blockers, anticoagulants, or anticholinergics
- Have chronic obstructive pulmonary disease
- Have musculoskeletal impairments/injuries that cause more pain during exercise than is tolerable
- Have a history of allergies to electrode gel, adhesive or alcohol
- Have recently experienced a concussion, or have had more than one concussion in the past
- Cardiorespiratory conditions that may prevent maximal exertion or wearing a mask during exercise

- **Cap used to monitor your brain function.** **Mask worn during the exercise test.**

WHAT WILL YOU BE ASKED TO DO?

If you agree to participate, you will be asked to attend up to three sessions in a kinesiology lab at the University of Waterloo. These visits will be 1.5 to 2.5 hours in duration. These visits will take place approximately 2 weeks apart. You will be carefully monitored during each session.

Prior to or on the first visit, you will sign this consent form and complete an exercise screening form.
You will be asked to refrain from exercising or ingesting caffeine or other stimulants day of your scheduled study sessions

The first visit will take 2.5 to 3 hrs. You will complete the Physical Activity Readiness Questionnaire (PAR-Q+). This questionnaire will be used to ensure that it is safe for you to participate in physical activity. You will also complete the International Physical Activity Questionnaire (IPAQ) to assess the amount of physical activity you are regularly involved in.

Resting heart rate and blood pressure will be taken prior to the start of each study session with a commercially available blood pressure cuff. Heart rate will additionally be monitored throughout the study session using a chest strap that will record heart rate and display the information on a watch.
We will then monitor your brain activity while you perform a computer based cognitive task. Response time and response accuracy will be measured from this task. The Stroop task will require that you respond to words presented on a monitor. You will be asked to respond based on whether the colour of the word matches the colour that the word represents. Errors are normal on these tests and should not be taken as a reflection of your cognitive abilities. You will wear a cap with electrodes that will monitor your brain function during this test. A picture of the cap is shown above. The cap contains many disks that sit on the surface of your scalp. Several electrodes will also be placed on your face to measure eye-blinks while your perform the Stroop task.
Prior to testing, we need to clean the sites underneath each of the disks and move the hair out of the way. This is done using a disposable blunt syringe, which is not sharp and is about as wide as a pen tip. This blunt syringe is also used to squirt a small amount of gel onto your scalp to improve the signal from your brain activity.

During the first session you will asked to perform a graded exercise test to measure aerobic fitness level. During this test, you will perform increasingly more difficult exercise intensities on a reclined stationary bicycle until you reach your maximum level. You may choose to stop at any time. During this test, the gases you breathe will be monitored through a facemask and computer system. Your heart rate will be monitored with a chest strap throughout the exercise test. You will likely be fatigued after the session and may have sore muscles the next day. You will be required to perform a sufficient cool down following the test, and your heart rate and blood pressure will be taken at the end to ensure that these values return to resting levels before you leave the lab, to ensure your safety. If you feel any unusual discomfort or pain or if you feel dizzy, faint, or light headed during this test, inform the researcher immediately and the test will be stopped. You will be provided a towel and shampoo to wash your hair, if you wish, at the end of this study session. All equipment and devices used throughout the study will be properly cleaned and disinfected prior to each use.

In the second and third sessions, you will perform approximately 20-30 minutes of exercise on a reclined stationary bicycle. How hard you exercise in these sessions will be carefully set and monitored. You will be free to stop at any time. The exercise intensity for each of these sessions will be individualized to you so that the exercise will be reasonable according to the values obtained from your graded exercise test. Exercise intensity will be reviewed by someone trained in exercise prescription to ensure your safety. The two exercise protocols used will be a high intensity interval training session (HIIT) and a moderate intensity continuous training session (MCT). The HIIT session will require that you cycle at high levels for short periods of time interspersed with periods of active rest. The MCT session will require that you cycle for 22.5 minutes at a moderate intensity. Both protocols will include sufficient warm-up and cool-down periods to prevent injury and ensure recovery. You will perform the Stroop task both before and after each exercise session, while your brain activity is monitored. The second and third sessions will take approximately 2 hours.

All study sessions will be performed in the Brain and Body Lab which is in the B.C. Matthews Hall, Room 1015 at the University of Waterloo.

HOW MUCH TIME WILL IT TAKE?

Your first visit will be approximately 2.5 hours.
Your second and third visits will be approximately 2 hours each.
The total time commitment for this study is approximately 7 hours.

PARTICIPATION

If you choose to participate, we recommend wearing light, comfortable clothing and running shoes to the study sessions. You will be asked to refrain from exercising or ingesting caffeine or other stimulants on the day of your scheduled study sessions.

Participation in this study is entirely voluntary and you may refuse to participate or withdraw at any time by informing the researcher. You may also decline to answer question(s) or stop taking part in the study tasks at any time by notifying the researcher. Likewise, the researchers may also stop participation at any time should an irregularity be observed (e.g. irregular heart rate). If we learn any new information that might affect your desire to participate or decision to remain in the study, you will be told of this.

RISKS

You may experience temporary muscle fatigue or soreness from the exercise. There is also a small chance that chest pain (cardiac ischemia) or heart beat irregularity (arrhythmia) will occur. You will only be included in the study if you are considered to be at low risk for such events. In addition, we will stop the exercise if you report chest pain, shortness of breath, drowsiness, feeling faint, dizziness, or lightheadedness. Heart rate will be monitored continuously to detect any abnormal changes. You will be under direct supervision by an individual trained in first aid and CPR for the entire study to ensure your safety.

You may experience mild pain or discomfort when we clean your skin using abrasive gel so that we can monitor your brain activity. If you have sensitive skin, you may develop a slight reddening from the adhesive used to affix some electrodes to the skin. Your head may also be slightly sore from wearing the EEG cap. Electrode gel will get into your hair as a result of the EEG cap, but soap, shampoo, conditioner and towels will be provided if you wish to wash your hair in a nearby changing facility. The researcher will ask you if you have any known allergies or sensitivities before beginning the procedures. The EEG cap will be thoroughly cleaned with soap and hot water after each session. The blunt syringes will be properly disposed of immediately after use.

BENEFITS

By participating in this study, you will benefit by furthering your knowledge and understanding of experimental procedures commonly used in neuroscience research. Your help will contribute to

our knowledge on the benefits of aerobic exercise to brain health. This study may provide insight for future research on stroke rehabilitation and prevention of cognitive impairment, particularly research on neuroplasticity (the brain's ability to adapt).

CONFIDENTIALITY AND SECURITY OF INFORMATION

Your identity will be kept confidential and will not be passed to a third party. Only the researchers associated with the study (Spencer Wikkerink and Dr. Middleton) will have access to the data. The collected data will be coded with participant numbers (not names) and will be kept in a locked file cabinet in Burt Matthews Hall room 1015 or on a password-protected computer for seven years after publication. After this time, all paper copies will be shredded and computer disks erased.

QUESTIONS

Any questions with regard to this research should be directed to Dr. Laura Middleton, 519-888-4567 Ext. 33045.

ETHICS CLEARANCE

This project has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee. However, the final decision about participation is yours. Participants who have concerns or questions about their involvement in the project may contact the Chief Ethics Officer, Office of Research Ethics at 519-888-4567, Ext. 36005 or maureen.nummelin@uwaterloo.ca.

UNIVERSITY OF WATERLOO

Student Investigator
Spencer Wikkerink, BSc

Faculty Supervisor
Laura Middleton, PhD

CONSENT FORM

Physical Activity and Cognitive Function

By signing this consent form, you are not waiving your legal rights or releasing the investigator(s) or involved institution(s) from their legal and professional responsibilities.

I have been informed of the aim of this study, and have read the INFORMATION AND CONSENT FORM. I am aware that I am under no obligation to take part and may withdraw from the study at any time.

I am aware that the researchers will be asking me questions concerning my health. This information will remain confidential and I will be free to refuse to reply to any question that I may prefer not to answer.

I am aware that I am free to ask questions and to withdraw from this study at any time. I am also aware that, if I feel uncomfortable during exercise, I may ask the researcher to stop it immediately.

I am aware that by signing this consent form, I am not waiving my legal rights, nor does it relieve the investigators or involved institution from their legal and professional responsibilities.

I agree to take part in the study. I will receive a copy of the signed consent form.

_____
PARTICIPANT NAME

_____
PARTICIPANT SIGNATURE

_____
LOCATION

_____
DATE

_____
WITNESS

Appendix E

International Physical Activity Questionnaire (IPAQ)

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (October 2002)

LONG LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation

Translation from English is encouraged to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective.* Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

   ☐ Yes

   ☐ No → ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

   _____ **days per week**

   ☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

   _____ **hours per day**
   _____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

   _____ **days per week**

   ☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**
_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**
_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

_____ **hours per day**
_____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**
_____ **minutes per day**

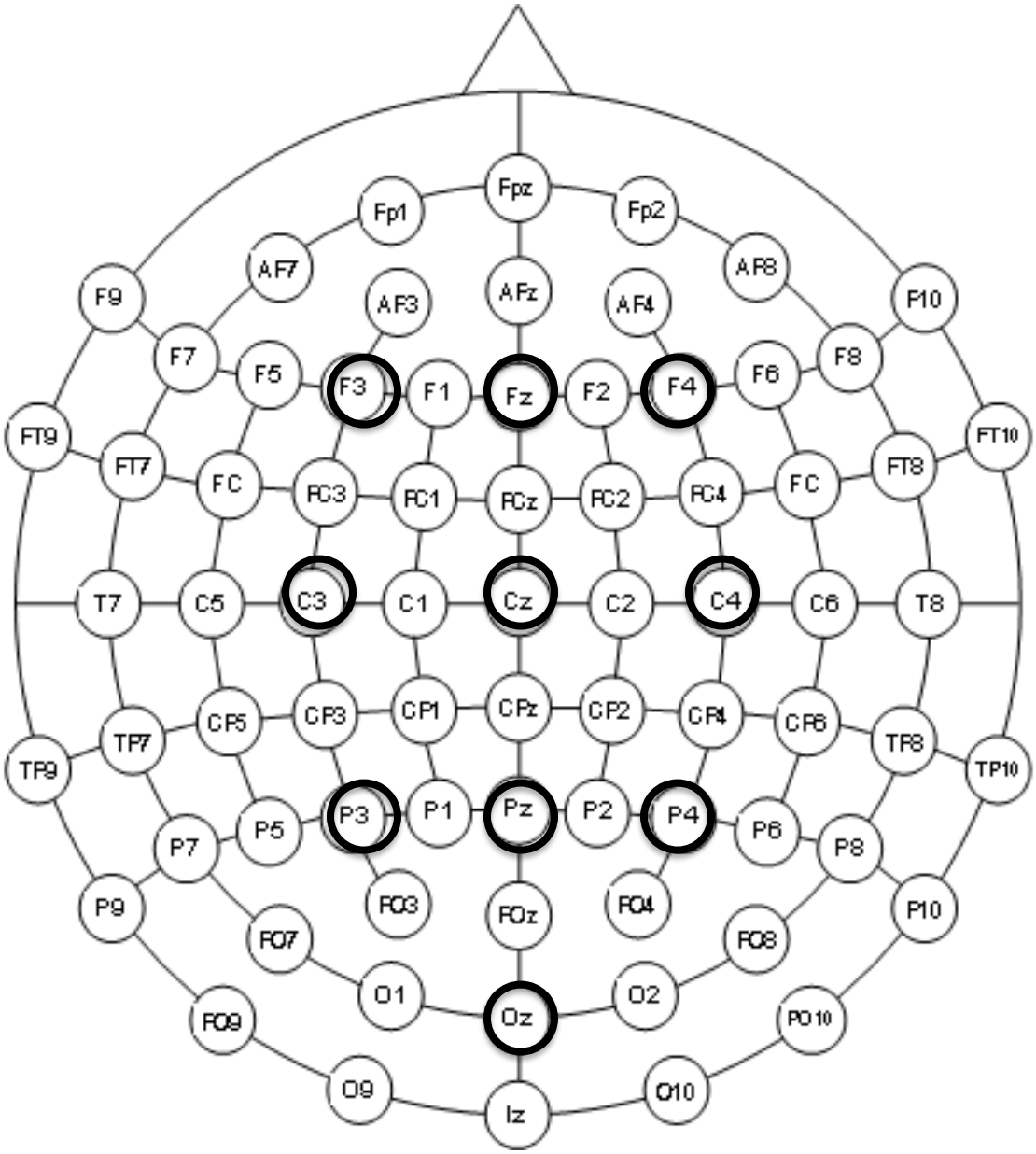
27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**
_____ **minutes per day**

This is the end of the questionnaire, thank you for participating.

Appendix F

EEG Electrode Schematic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