Investigating the effects of exercise on attentional correlates in those with a history of concussion

by

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Authors 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

The current understanding of changes that occur neurophysiologically and neurocognitively in the brain following concussion are considerably debated among researchers. Even more largely debated are the long-lasting changes to brain structure and function as a result of neuronal damage. Recently there has been a paradigm shift that includes analyzing these physical changes in the brain and their implications on long-term health. Recently, studies have begun to look at long-term changes and their implications in the exacerbation of accelerated cognitive aging. Findings show that early in the aging process, those who have previously sustained concussions have brain wave patterns that match those of older adults, including those with Alzheimer's. It was hypothesized that those who had previously sustained a concussion, following a bout of moderate intensity exercise, would have increases in both the P3 and N2 amplitudes compared to non-concussed counterparts. Eight participants were collected and assigned to a concussion (C) or non-concussion (NC) group based on their concussion history. Participants were asked to complete a novelty oddball paradigm during which targets, non-targets, and novel stimuli (images) were shown in randomized blocks. Participants were required to respond to targets, ignore non-targets, and remember the number of images and what the images were. Following this task, participants exercised for 20 minutes at 70% of heart rate max and rested for 10 minutes post-exercise before participants completed the same task, this time with different novel stimuli (targets and non-targets remained the same). P3 and N2 amplitudes and latencies were measured using electroencephalography to investigate the neural correlates related to attention. To assess behavioural changes, response time and accuracy were collected during stimulus presentation. ERSP data was also collected to explore oscillation patterns in the concussed brain before and after exercise. Due to factors related to COVID-19, supplementary data sets were used to explain pre-exercise P3 and N2 amplitudes, as well as, ERSPs.

Results show that participants who had previously sustained a concussion exhibited larger amplitudes in the P3 and N2 waveforms pre-exercise, as opposed to their NC counterparts. Following exercise however, while the NC group increased in amplitude as expected, the C group decreased in amplitude in such a way that matched levels similar to control data, a finding inconsistent with previous studies done with concussion and exercise. Coincidentally, ERSPs showed decreases in synchrony in theta, alpha, and beta bands following exercise in the NC group, while the C group exhibited the opposite: increases in synchrony following exercise.

Our results suggest that there are long-standing structural and functional changes to the brain following concussion and depending on the individual history of each event, can inflict differential results on the neural markers of attention. Additionally, there may be a relationship between long-term exercise and adaptations to concussion wave patterns in attention that could aid in the slowing of accelerated aging in the brain following concussion. These results inform brain wave patterns in concussion following exercise and future studies in aging populations who have previously sustained a concussion.

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List of Abbreviations

AP	Antero-posterior
C	Concussion
CHI	Closed Head Injury
DLPFC	Dorsolateral Prefrontal Cortex
DMN	Default Mode Network
EEG	Electroencephalography
ERP	Event Related Potential
ERSP	Event Related Spectral Perturbation
fMRI	Functional Magnetic Resonance Imaging
GABA	Gaba Aminobutyric Acid
GAQ	Get Active Questionnaire
HR	Heart Rate
IAPS	International Affective Picture System
IPAQ	International Physical Activity Questionnaire
ML	Medio-Lateral
mTBI	Mild Traumatic Brain Injury
N	Novel
NC	Non-Concussed
NT	Non-Target
PFC	Prefrontal Cortex
PPC	Posterior Parietal Cortex
RPE	Rate of Perceived Exertion
SSS	Stanford Sleepiness Scale
T	Target
TBI	Traumatic Brain Injury
TMT	Trail Making Test
TRN	Thalamic Reticular Nucleus

1.0 Introduction

The current understanding of changes that occur neurophysiologically and neurocognitively in the brain following concussion are considerably debated among researchers. Even more largely disputed are the long-lasting changes to brain structure and function. Only in the last several years that researchers have begun to look at the potential for these continuing effects and their implications on long-term cognitive health. It is possible that a single injury has the potential to leave long-lasting and sustained alterations to brain structure and function, even when symptoms are no longer present.

The thalamus and prefrontal cortex (PFC) are critically and functionally imperative for normal cognition. Both structures act to filter incoming sensory stimuli based on the relevance to a given task or goal. This process is also known as sensory gating and is thought to spare the cortex from a seemingly endless barrage of sensory information, giving precedence to information that is most important. Thus, sensory gating is a prime candidate for long-term post-concussive impairment.

Although there has been limited research on the long-term attentional effects of concussion, there has been extensive research to suggest that exercise can alter these attentional correlates. Through acute neuroplasticity, an acute bout of aerobic exercise has the ability to increase both P3 and N2 event-related potential (ERP) amplitudes. The P3 is a parietally maximum positive wave that depends strongly on the cognitive processes involved with a specific task and reflects task relevant stimuli being attended to. The amplitude is correlated with the amount of attentional resources allocated to a given task and latency is associated with neural efficiency. Conversely, the N2 is a fronto-central negative peak that can be interpreted in the presence of effortful controlled stimulus processing. The peak latency is associated with the time

taken to categorize the stimulus being elicited and the amplitude is correlated with the novelty of a stimulus that is salient but unrelated to task goals. However, the literature on sensory gating post-concussion and exercise as a form of long-term rehabilitation is sparse, and the few investigations that have been employed suffer from critical flaws. Mainly, the lack of case-by-case analysis of those with a history of concussion. Because of the individuality of a concussion history, averaging groups of those with concussion may mask changes that would have otherwise been present.

Broadly this thesis aims to further the understanding of exercise as a tool for priming neuroplasticity in the brain specifically with regards to long-term changes in attentional correlates following a concussion. A neurophysiological approach will be taken, using electroencephalography (EEG) to record the neural activity of early processing stages produced within attentional systems, such as the dorsal attentional network. An exercise intervention will place specific emphasis on the facilitation of neuroplasticity of certain brain structures and as a result, cognitive functioning including attention, in an attempt to gather information relating exercise to probable permanent neural changes following concussion.

2.0 Literature Review

2.1 Concussion

2.1.1 Definition and Epidemiology. Traumatic brain injury (TBI) is a major cause of death and disability. According to Dewan and colleagues (2018) it is estimated that there are 69 million new cases of TBI seen worldwide each year. Mild traumatic brain injuries (mTBI) specifically, account for more than 75% of all head trauma cases reported annually (Grossman & Inglese, 2016) making mTBI/concussions the most common type of acquired brain injury (Sussman et al., 2017). It is likely however, that these numbers are exceedingly low, as it is estimated that between 25-42% of concussions go unreported (Patterson & Holahan, 2012). Numerous costs have been placed on society including hospital bills and loss of productivity (Kruijk et al., 2002). This physical and economic burden has created a silent epidemic (Banks et al., 2016; Grossman & Inglese, 2016; Howell et al., 2012; Patterson & Holahan, 2012) caused by unseen traumatic biomechanical forces (Thériault et al., 2009) that can generate often complex instantaneous and transient impairment to mental functioning (Sussman et al., 2017). However, new research suggests that the impairments following concussions might not always be transient (Broglio et al., 2012).

A concussion, as agreed upon by the International Conference on Concussion in Sport, can be defined as "the complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces" (Aubry et al., 2001). These traumatic biomechanical forces can occur as a result of direct or indirect impact, rapid acceleration or deceleration, or intense changes in pressure (Patterson & Holahan, 2012). Following an insult to the head there are a wide range of symptoms that may occur including: headache, nausea, vomiting, dizziness, fatigue, abnormal sleeping patterns, drowsiness, and more (Aubry et al., 2001). Because of the

wide range of symptomology concussion has become one of the most difficult injuries to both diagnose and manage (McLeod et al., 2017).

The clinical symptoms that present themselves represent the functional manifestation of a currently undetectable structural injury (Kaltiainen et al., 2018). Concussions may result in unseen structural damage caused by cellular apoptosis and atrophy (Sussman et al., 2017) and due to lack of neural regeneration in the brain, connections can be permanently lost (Menon, 2015). Currently, none of the symptoms, signs, or objective clinical tests offer enough sensitivity or specificity to diagnose concussion. All present-day clinical tools assess the secondary manifestations of concussion rather than the underlying complex pathophysiological processes affecting the brain (Eckner et al., 2016). Because current instruments lack the necessary sensitivity to detect subtle cognitive decrements in the post-acute stage of injury and the symptom set and severity varies from person to person (Broglio et al., 2009), management strategies for rehab are extremely difficult to mandate.

Despite the confusion and uncertainty, researchers can agree, a shift in how concussion is thought about and researched needs to be made. More attention needs to be placed on the associated risks that come with repetitive concussions and the additive damage that may occur to brain structure and function. The focus needs to be expanded from the incidence of multiple concussions to the potential risks associated with cumulative impact exposure (Broglio et al., 2012; Talavage et al., 2014) and lastly, the view of concussion needs to be broadened to understand the effects of injury across a lifespan (McAllister & McCrea 2017).

2.1.2 Short-Term Neurophysiological Effects. When suffering a head impact that results in a concussion there are a variety of symptoms and effects that occur directly after and during symptom resolution. The link between head impact and white matter diffusion measures

suggests a causal relationship between the magnitude and timing of head impacts, as well as changes in white matter measures in some brain regions. These changes may also be related to verbal learning, memory, and executive function (McAllister et al., 2013). Following an impact, it has been shown that as early as one day after concussion there is increased functional connectivity in some regions of the brain (Militana et al., 2016). As well, there is a common trend following concussion toward a decrease in thalamic volume, increased inflammation and reduced perfusion (Banks et al., 2016). Cubon and colleagues (2011), through diffusion tensor imaging, demonstrated that patients with moderate-to-severe brain trauma displayed smaller thalamic volumes due to damage throughout the thalamic radiation than those with lesser brain trauma. They interpreted these results to mean that in the presence of cortical lesions, the thalamus may become susceptible to trans-neuronal degeneration (Shin et al., 2014; Grossman & Inglese, 2016). Ross and colleagues (1993) identified selective neuronal loss in the thalamic reticular nucleus in post-mortem patients that had previously suffered from severe brain trauma. They also noted that because the thalamic reticular nucleus is a gamma-amino butyric acid (GABA) population of cells which project to other thalamic nuclei, the damage must have come from a mechanism unrelated to axonal tearing (Grossman & Inglese, 2016). In addition, Talavage and colleagues (2014) found decreases in functional magnetic resonance imaging (fMRI) activation levels in the dorsolateral prefrontal cortex and cerebellum during working memory tasks. Although these results represent the damage of moderate to severe TBI, current anatomical and physiological consideration, as well as advance imaging and animal modeling, might suggest that the thalamus might play a significant role in impairment caused by mTBI (Grossman & Inglese, 2016).

Shin and colleagues (2014) also carried out an experiment in athletes who participated in either boxing or MMA. They determined that increased exposure to professional fighting was associated with lower brain structure volumes, particularly in subcortical structures. The most consistent decrease in volume of these structures, was in the caudate and thalamus. When correlated with speed of processing time, the researchers found that smaller volumes in the thalamus were related to lower speeds which may have been caused by increased neural inefficiency. The researchers concluded that neuronal loss in the subcortical grey matter structures could be a result of axonal tearing and further Wallerian Degeneration following concussion. In addition, torsional forces could produce fluid waves that traverse through the lateral ventricles and could conceivably reach and injure deeper cortical structures (Shin et al., 2014). However, the design of this study does not directly test the conclusions made by researchers and these are merely suggestions.

In a study done by Sussman and colleagues (2017) male participants were recruited for neuromorphological testing. The purpose of this study was to examine whether a single injury induced measurable changes in morphometry. They found reductions in white matter volume and mean cortical thickness following a single concussion that was independent of age or intelligence. They speculated that the reductions in white matter volume may hinge on tract disruption due to stretching, inflammation, crushing and separation from the gray matter, promoting deafferentation and demyelination of axons. This view is supported through diffusion tensor imaging (McAllister et al., 2013; Sussman et al., 2017). In a lobe-based analysis done by Sussman (2017), it was found that there was reduced cortical thickness that was located in primarily left frontal regions. These areas play a role in executive function, including working memory, mental flexibility, attention, and inhibition and may be a prime candidate for

perturbation following concussion. These findings suggest there are large-scale and almost immediate remodelling of some cortical structures that underlie the neurobiological bases of the transient cognitive sequelae of concussion. White matter disruption in the form of axonal shearing, can induce Wallerian Degeneration and concomitant reactive astrocytosis that would contribute to gray matter atrophy (Sussman et al., 2017).

In a study done by Rugg and colleagues in 1988, researchers looked at the N2 and the P3 ERP in an auditory oddball task in closed head injuries (CHI). The N2 component provides an electrophysiological index of moment-to-moment deployment of visual-spatial attention (De Beaumont et al., 2007). They found that the N2 latency was longer in patients with a CHI. The amplitude of the N2 wave was also larger in those with CHI. Conversely, they discovered that the P3 amplitude in CHI patients was smaller, but the latency was not significantly changed (Rugg et al., 1988). Unlike the N2 component, the P3 amplitude and latency is thought to relate to memory updating, subjective significance, and stimulus probability. The amplitude is also thought to positively correlate with the amount of attentional resources allocated to task demands. The P3 amplitude was suspected to be related to a worse performance on memory tasks and memory updating (De Beaumont et al., 2007). Thériault and colleagues (2009) furthered this statement through a three-tone auditory oddball paradigm and discovered that P3 alterations that were a result of a concussion were not limited to the first few months or even years post-injury. Meaning that the alterations do not dissipate even though symptomology may. They also found that later in the concussion stages the P3 amplitude began to trend toward baseline. However, the signals did not fully return to baseline even up to one-year after concussion, but instead, remained depressed. Overall, this led researchers to believe that persistent reductions in P3 amplitude may reflect a reduced frontal lobe function efficiency that

particularly affects one's ability to shift attentional resources to novel stimuli (De Beaumont et al., 2007; Guay et al., 2018; Thériault et al., 2009).

Researchers, based on the longer latency of the N2 potential, concluded that the speed of processing, or the time required to categorize the eliciting stimulus was impaired. The delay in this component implies a dysfunction in categorization along with other later processes (eg. response selection) (Rugg et al., 1988). Rugg and colleagues also looked at the decreased N2 amplitude in CHI patients and saw an association with cognitive effort. The larger the amplitude in N2 the greater the cognitive demand of the stimuli (Ledwidge & Molfese, 2016; Rugg et al., 1988). This phenomenon could be predicted by a hypothesis set out by Van Zomeren (1984) titled "the coping hypothesis". This hypothesis states that "as a result of deficient information processing, CHI patients can cope with task demands only by the allocation of excessive cognitive effort" (Ledwidge & Molfese, 2016; Rugg et al., 1988).

Lastly, it is important to note that in addition to the ERP changes seen both directly following concussion and years later after symptom resolution, there are other long-standing changes that are seen in EEG recordings. Brain oscillations have been hypothesized to play a fundamental roll in neuronal synchronization across functionally connected brain regions (Guay et al., 2018). It is because of the extensive and wide-spread synchronization that event related spectral perturbations (ERSPs) have been thought of as prime candidate for damage following injury. Post-concussion has revealed a number of changes including, decreases in beta, alpha, and gamma waves, and an increase in theta desynchronization. A study done by Guay and colleagues (2018) revealed a significantly reduced alpha band frequency between 350-550 ms post stimulus which was commonly associated with a concomitant increase in the theta-alpha frequency ratio. These results were seen in patients up to 12-months post injury (Barlow et al.,

2018; Guay et al, 2018). In addition, these results correlated strongly with the number of clinically sustained concussion and the amplitude of the P3 waveform component (Guay et al., 2018). An increase in P3 amplitude, is usually recorded in conjunction with a decrease in alpha amplitude.

In another study done by Barlow and colleagues (2018), both theta and beta oscillations were measured in depth. The researchers discovered that following concussion there was greater theta desynchronization and lesser beta desynchronization which was determined following task-switching (Barlow et al., 2018). Finally, in a study done by Munia et al., (2017), ERSP data was collected in high school athletes following concussion and a decrease in beta waves as well as, a decrease in gamma power was found. It was concluded that this may point to less effective local neuronal synchronization to external stimuli in thalamic sensory oscillations (Munia et al., 2017). These changes may result in a decrease in proactive control and an inability to filter appropriate incoming information efficiently.

2.1.3 Long-Term Neurophysiological Effects. Recent work done by various researchers has demonstrated cognitive decline, neurobehavioral changes, neurodegenerative disease, electroencephalographic and motor control changes in otherwise healthy individuals with a history of concussion (Broglio et al., 2012; McAllister & McCrea 2017). Years later following the 'resolution' of concussion there are changes seen in the brain of those with a concussion history. More specifically, diffuse amyloid plaques, as well as sparse neurofibrillary tangles and tau positive neuretic threads were found in neocortical areas. When reviewing previous and current data Broglio and colleagues (2012) hypothesized that both concussive and subconcussive head impacts set about a 'cascade of pathological events that accelerates decrements in cognitive function that are typically associated with the aging process'. The underlying theory that this

group of researchers was trying to explain involves cognitive reserve. Cognitive reserve simply put, is the brain's ability to improvise and find alternate ways of getting the job done. Those with an injury history can rely on their cognitive reserve to maintain a high level of functioning with no observable clinical deficits. Instead, alternate pathways are recruited to achieve the same end goal without behavioural deficits. Neural networks are thought to reorganize post-concussion through the development of new local and distal networks to compensate for the previously mentioned reductions in neural efficiency. This allows those with a concussion to achieve similar performance levels to their non-concussed counterparts (Guay et al., 2018). It is thought that 'those with a denser gray matter, a high number of neuronal connections, and with a more robust neural network can better afford to lose a fixed amount of ability before demonstrating a clinically meaningful decline' (Broglio et al., 2012). Both concussive and subconcussive head traumas are thought to intensify the aging process by decreasing cognitive reserve at a faster rate, ultimately leading to premature cognitive dysfunction (McAllister & McCrea 2017).

During the 'normal aging process' there is typically an overall decrease in cortical gray matter density and similar regional specific declines in white matter volume seen. There have also been decreases in synaptic plasticity, dendritic spine density, calcium homeostasis, and the expression of neurotrophic factors observed. Additionally, there have been perturbations in the function of dopaminergic, serotonergic, cholinergic, and glutamatergic circuits (Broglio et al., 2012). Behavioral consequences of the physiological changes mentioned are deficits in memory, attention, orientation, motor function, reaction time, and balance regulation.

Combined, the attentional resource decrements and decreases in cognitive reserve seen following concussion mimic what is seen in older adults transitioning from a stage of mild cognitive impairment to Alzheimer's disease. In addition to presenting with Alzheimer's, older

adults have a noticeably smaller P3 amplitude and a prolonged latency. Research done by Piirtola & Era (2006) built upon these findings, and as a result, found that concussion may also influence motor control. They determined that those with a concussion history have a 16.5% decrease in medio-lateral (ML) balance complexity and a 29.0% increase in antero-posterior (AP) complexity indicating a shift in the balance strategy of those with a concussion history. In older adults, less control over the ML sway has been correlated with an increased risk for falls (Piirtola & Era 2006). As such, the cognitive and motor changes observed in those with a history of concussion may set the stage for disease states seen in an older adult population (Gironell et al., 2005; McAllister & McCrea 2017).

2.1.4 Neurocognitive Effects. As mentioned previously, functional connectivity refers to the functionally integrated relationship between spatially separated brain regions and, when damaged, can lead to decreases in processing time. Successful interaction with the environment hinges on the ability to extract the relevant sensory information from an overwhelming amount of continuous sensory input (Brown et al., 2015). More specifically the thalamus helps to determine salient information with regards to task demands and has direct links to the default mode network (DMN) and widespread motor networks. The DMN and motor networks are critical in coordinating and routing information in the brain. They serve functional and specialized purposes, such as visual perception, directed attention, and self-referential processes in the DMN (Dunkley et al., 2018). In addition, the DMN mediates processes related to memory, future thoughts, and attentiveness and is active when the brain is at rest (Dunkley et al., 2018; Militana et a., 2016). Militana and colleagues (2016) found the medial DMN to be particularly sensitive to concussive forces specifically with regards to functional connectivity. They theorized that the increases in functional connectivity being seen could be related to the use of cognitive

reserve following concussion and that other pathways are recruited to supplement the ones that have been damaged (Broglio et al., 2012).

Dunkley and colleagues, on the other hand, sought to determine changes in resting brain connectivity that may be mediated by oscillations in established intrinsic brain networks following concussion. They had originally predicted that connectivity would be reduced in concussion across multiple frequency scales and particularly that of the DMN (Dunkley et al., 2018). However, what they found was similar to that of Militana and colleagues (2016). They determined that there were significant increases in DMN connectivity in both the alpha and beta ranges in the concussion group compared to controls, which may be a reflection of an inability to disengage the DMN in response to task-shifting demands. Contrastingly, the motor networks looked at showed multi-scale network dysfunctions, concluding that this may be a result of neural circuitry changes, possibly related to GABAergic action and concentration. The course of reason behind these changes stems from how neural oscillations are thought to be managed. Management is believed to occur through a relation between excitatory and inhibitory neurotransmission that is related to resting GABA concentrations. The increases in DMN connectivity in beta amplitude within the motor networks, is thought to reflect an increase in cross-regional inhibitory processes (Dunkley et al., 2018). In agreeance with Broglio et al., 2012, Dunkley and colleagues (2018) concluded that the increases in connectivity seen could be a result of compensation for injury. More specifically, the hyperconnectivity found could be representative of the recruitment of additional resources to maintain cognitive function (Dunkley et al., 2018).

2.2 Overview of Attentional Systems

The neuroanatomical and regulatory capacity makes the PFC ideally suited to subserve human cognition (Knight et al., 1999). The PFC is crucial for integrative behaviour and involves both inhibitory and excitatory control of distributed neural activity in posterior brain regions. Knight and colleagues (1999) performed a review of studies that overviewed the inability of prefrontal patients to suppress responses to irrelevant stimuli in a range of sensory, motor and cognitive processes which provides evidence of an early sensory filtering mechanism in humans. Lastly, stimulus discriminability has been shown to be dependant on the degree of attention related evoked potential enhancement, providing a link between physiology and attention in humans (Knight et al., 1999). Later in the processing stream the PFC feeds into the thalamus providing a link between attentional structures.

The thalamus functions as a sensory relay center that has multiple thalamic nuclei that are interconnected with various cortical regions (Banks et al., 2016; Grossman & Inglese, 2016; Mitchell, 2015). However, Mitchell (2015) later discovered that each thalamic nucleus, more than likely, has a distinct functional relay role. The mediodorsal nucleus, as well as the anterior thalamic nucleus have dense inputs from the medial PFC areas and are implicated in higher-order cognition (Mitchell, 2015; Wright et al., 2015). To build upon this thought Nakajima & Halassa (2017) suggest that the thalamus also functions to control the functional connectivity with and across brain regions through the essential role of transmitting information within and between sensory, motor, and associative regions. Lesions of the higher-order thalamic nuclei have been shown to impair several cognitive functions including memory, attention, perception, and sensory-guided action (Saalmann, 2014). The lesions also perturb cortical-cortical information transmission. The thalamus itself has been found to be susceptible to injury, specifically, in TBI

or concussion. Commonly, changes in functional connectivity have been studied after concussion as a potential neurophysiological biomarker of injury (McAllister et al., 2013; Militana et al., 2016).

To discuss more in depth the importance of the thalamus in attention it is necessary to understand how it is structured. There are two types of thalamic relays that have been proposed. The first is a 'first order thalamic relay', which transmits sensory inputs from the periphery through ascending pathways to their interconnected cortical targets. The second is a 'higher-order thalamic relay'. Cortical inputs to thalamic nuclei that originate in layer V are referred to as 'driver' inputs and can transmit an already processed cortical message across other cortical areas depending on the characteristics of the glutamatergic receptors (Mitchell, 2015; Sherman, 2015). Higher order thalamic nuclei receive major input from cortical layer V as well as cortical layer VI and project to the cerebral cortex to form prevalent cortico-thalamo-cortical pathways providing an indirect connection between cortical areas via the higher-order thalamus (Saalmann, 2014). The two types of relays are reciprocally interconnected to the association cortex through cortico-thalamo-cortical connection and receive very little, if any, sensory input. Rather, their main inputs have been shown to originate from layer V of the cortex (Mitchell, 2015; Saalmann, 2014; Sherman, 2015). Because of this specific input pattern, the 'higher-order relay' pathways can carry previously processed cortical information onto other cortical areas (Mitchell, 2015). Higher-order relays also receive information from other cortical and subcortical inputs that have either an excitatory or modulatory function. These inputs include cortical layer VI, thalamic interneurons, the reticular nucleus, and other structures of the forebrain, midbrain, and the brainstem (Mitchell, 2015; Sherman, 2015).

When discussing inputs from cortical layer VI, there is either direct activation or inhibition of relay cells (Sherman, 2015) for autoregulatory feedback (Guillery et al., 1998). When the inputs are removed, elimination is seen of both direct excitation and indirect inhibition. Interestingly, layer VI corticothalamic cells' axons not only innervate the thalamus, but also layer IV of the cortex, suggesting that corticothalamic cells can affect transmission from its thalamic source as well as at its cortical target (Sherman, 2015). The higher-order thalamus may synchronize one network of cortical neurons and desynchronize other cortical networks, thereby selectively transmitting behaviourally relevant information between appropriately synchronized cortical neurons. This offers the advantage of dynamically routing information across the cortex according to the behavioural demands by synchronizing the necessary networks of neurons at different times (Saalmann, 2014).

In addition to the actions mentioned above, the thalamus also functions to tune the relevancy of incoming information. Behavioural flexibility requires that an organism disengage from a previously relevant stimulus and respond to a stimulus that has been presently experienced as irrelevant (Wright et al., 2015). Neural specificity of attentional processing is required for promoting relevant inputs over distractors (Nakajima & Halassa, 2017). The cognitive capacity for such switching involves: attention to relevant stimuli, suppression of irrelevant information, and adaptation to changing contingencies (Wright et al., 2015). In a study done by Brown and colleagues (2015), movement-related gating through task-relevancy effects was looked at. Through continuous theta-burst stimulation over the right dorsolateral prefrontal cortex (DLPFC) to lessen excitability, the modulation of movement-related gating levels that are normally present, were reduced. This supports the common idea that the DLPFC is partially responsible for modulation of movement-related gating. During relevancy-based gating there is

both selective inhibition and facilitation. It is also thought that there is specific facilitation of task relevant demands and inhibition of information irrelevant to the task at hand. It was Brown and colleagues that presented the idea that this mechanism is subserved by the DLPFC in conjunction with cortical contributions from the thalamic reticular nucleus (TRN) through both inhibition and disinhibition during gating.

The TRN itself has been commonly referred to as a sieve rather than a gate. The nucleus has been found to be divided into several distinct sectors, each related to a particular functional group of thalamocortical pathways. Afferents that exit the TRN and go to the thalamus (higher order nuclei) play crucial roles in controlling the firing patterns (tonic or burst) of thalamocortical relay cells to other brain regions (cortex). Notably the TRN has numerous sectors that each provide a nexus of interaction for several thalamocortical and corticothalamic circuits. These interconnections provide a place where many cortical areas concerned with one modality can interact (Guillery et al., 1998). The TRN then selectively inhibits or disinhibits the information sent through it based on the attentional feedback that is provided by the DLPFC in movement related gating (Brown et al., 2015). A specific example is when the DLPFC is attending to a specific stimulus. When the attention is shifted, excitatory projections synapse onto GABAergic cells in the TRN, which through interneurons, might lead to disinhibition or facilitation of the relevant stimuli, resulting in increased sensory transmission through the necessary pathways (Brown et al., 2015; Knight et al., 1999). Although this novel information is interesting, it does have its limitations as the above conclusions are simply speculations. However, the conclusion from Brown and colleagues (2015) can provide, in part, details about the thalamus and its responsibility and role in augmenting the relevant information in an overly hectic environment, all while suppressing the irrelevant (Brown et al., 2015).

2.3 EEG, ERPs, ERSPs

2.3.1 Technique and Definition. Commonly used to investigate the brain mechanisms underlying attentional processes are ERPs from EEG analysis (Ledwidge & Molfese, 2016; Rusiniak et al., 2013; Thériault et al., 2009). ERP research is a non-invasive way to provide insight into the stages of early sensory processing that guide behaviour. An EEG cap allows averaged electrical brain responses to be collected as ERPs, allowing one to determine the time course of higher-level processes such as attention and memory updating in the human brain tied to a specific stimulus presentation (De Beaumont et al., 2007). The cap itself houses electrodes that can be used to pick up electrical activity that reaches the scalp. The analog signal picked up by the cap is converted into a digital signal and the signal is epoched to relevant events. Lastly, epochs are averaged across events to obtain usable data. The electrodes measure the synchronized synaptic activity of neural networks with high temporal resolution. As such, ERPs present a viable option for assessing the apparent electrophysiological disruption following concussion (Eckner et al., 2016). To differentiate between normal and concussive processing an oddball paradigm that elicits a rare stimulus is commonly used to enhance the fronto-central negative peak – N2, and a subsequent parietally-maximum positive wave – P3 (De Beaumont et al., 2007; Ledwidge & Molfese, 2016; Rugg et al., 1988), both of which are commonly present when attentional processing is required.

2.3.2 Neural Generators. The N2 wave has been interpreted in the presence of effortful, controlled stimulus processing with a peak latency that correlates with the time taken to categorize the stimulus being elicited (Ledwidge & Molfese, 2016; Rugg et al., 1988). More specifically the N2 component represents one's ability to monitor responses and inhibit inappropriate motor responses (Broglio et al., 2012). The N2 wave form is located primarily on

anterior scalp sites and is mediated by top-down cognitive control from the lateral prefrontal cortex. The N2 has been found to elicit roles in executive function, stimulus mismatch with a mental template, and conflict monitoring. The P3 conversely, is endogenous and depends strongly on the cognitive processes involved in a specific task. It is a positive deflection that appears under condition of uncertainty about the nature of the upcoming stimulus (Ledwidge & Molfese, 2016; Rugg et al., 1988; Rusiniak et al., 2013). Both the hippocampal formation and the thalamus influence the mechanisms underlying P3 generation with regards to both action selection and filtering of incoming information (Herrmann & Knight, 2001). The P3 component can be further subdivided into two components: P3a and P3b. The P3a component of the P3 is the more frontal early component of the ERP that reflects the automatic novelty of detection. This potential involves the anterior part of the temporal lobe, as well as the PFC (Barcelo et al., 2002) which can exert both excitatory and inhibitory control on the neural generators of early ERPs. Whereas the P3b involves the posterior portion of the parietal lobe (Herrmann & Knight, 2001). The P3b reflects the processing of task relevant deviant stimuli that are attended to (Rusiniak et al., 2013). The deviant stimulus represents that which is irrelevant to the task but is more salient than the targets themselves (eg. Novel stimuli in an oddball paradigm) (Polich et al., 2003). The P3 amplitude has been positively correlated with the amount of attentional resources allocated (the brain's ability to attend to salient information among competing signals) to a particular task and is thought to be a measure of stimulus classification speed. The peak latency, however, is negatively correlated with mental efficiency. Short latencies are associated with better performance on neurophysiological tests that assess rapid attentional resourcing (De Beaumont et al., 2007).

In addition to the ERP information presented from EEG, ERSP can be used to determine cerebral dysfunction in concussion. Event related spectral perturbations are a type of frequency analysis that can be further decomposed into sine waves. From this point temporal information can be transformed into delta (1-4 Hz), theta (4-6 Hz), alpha (8-12 Hz), beta (18-35 Hz), and gamma (over 35 Hz) bands, which provides a way to look at the processing dynamics of various groups of neurons. Due to the nature of ERSPs, they must be time locked to the presentation of a stimulus. This type of analysis measures the average oscillatory amplitude induced by the presentation of a stimulus relative to a pre-determined pre-stimulus period. When a stimulus is presented, there are variations in the spectral amplitudes that are thought to reflect changes in the activity of large assemblies of neurons. There are two types of changes that can be imposed. The first is event-related synchronization which occurs when the amplitude of a given frequency increases with stimulus presentation. The second, event-related desynchronization, occurs as a result of a reduction in amplitude in response to a stimulus (Guay et al., 2018).

Each band present in ERSP analysis represents a variety of cortical processes. In the lower frequency range, theta power is thought to be responsible for proactive control. This type of control is the means through which the brain prepares itself for an upcoming goal-directed behaviour. Alpha power on the other hand, has implications in cognitive efficiency, as well as visual and spatial attention and because of this has been known to decrease as a function of attentional demands reflecting the gradual release of inhibition associated with the activation of attentional networks during information processing (Guay et al., 2018). In other words, alpha band power represents cortical idling. In response to stimulation there is desynchronization that occurs, leading to an overall decrease in the alpha power. In concussion, the baseline level of alpha power is lower on average compared to non-concussed subjects (Herrmann & Knight,

2001) and being that an increase in alpha power is heavily tied to increased demands for attention, it is believed that this decrease in concussed patients may lend to the ERP changes seen in attentional tasks (Guay et al., 2018; Herrmann & Knight, 2018). Lastly, for the purposes of this experiment, beta power is thought to help maintain a current behaviour, which may stabilize the neural ensembles engaged for a given task (Guay et al., 2018). Beta power is also thought to play a role in episodic memory, decision making, and executive function (Barlow et al., 2018).

2.4 Relevancy Based Gating

The ability for a human to adapt behaviour in response to an ever-changing environment is critical to survival. In such an environment our senses are constantly being overloaded with sensory inputs that require our attention in order to guide neural resources to prioritize the processing of behaviourally relevant stimuli. Fundamental substrates of cognition, such as attention, are thought to arise from mechanisms such as action selection. In order for this to occur, top-down attention must first be activated as a guide to select sensory stimuli that are relevant to current behavioural goals, all while ignoring irrelevant distractors. Hence, when perceptual decisions are guided by attention, they are likely to be faster and more accurate (Huda et al., 2018).

This ability to adapt to various stimuli requires that we have an executive control system that allows us to respond flexibly to changing environmental contingencies; shifting attention among learned stimulus-response associations and choosing the correct action from a large behavioural repertoire (Barcelo et al., 2002; Huda et al., 2018). Classically, executive function has been defined as the ability to flexibly plan purposeful actions and is largely considered to be responsible for the synthesis of external stimuli and preparation for action. Therefore, attentional

processes are considered to be important elements of executive function. The aforementioned attentional tasks include decision making, troubleshooting, novel sequence of actions, and tasks considered to be technically difficult (Howell et al., 2012). Attentional performance is considered to be successful when the desired sensory channel is selected, focus on that input is maintained, and concurrent inhibition of distracting environmental information is performed (Yamaguchi et al., 2004). Specifically, attention permits us to focus on a subset of incoming sensory information, since the brain is not capable of processing all incoming sensory information at once (Herrmann & Knight, 2001). In a study done with animals, it was found that the animals reached a decision quicker on 'easy' trials (high evidence for one alternative) and responded slower on 'hard' trials with more ambiguous sensory evidence. The PFC and posterior parietal cortex (PPC) in the animals were found to be crucial nodes in a distributed network necessary for evidence accumulation. In conjunction with these findings researchers also discovered that attention strongly modulated the activity of neurons that represent the attended stimulus widely across the brain, including both cortical and subcortical structures (Huda et al., 2019).

The PFC, for years, has been thought to be a nexus that links perception and action selection through attention. Through modulation, it is thought that PFC activity may generate different behavioural strategies suited to the task demands (Huda et al., 2018). It was discovered that the PFC provided top-down signals that were necessary for observed attentional modulation of the visual cortex in a primate experimental group (Moore & Armstrong 2003). More specifically, the DLPFC is responsible for inhibiting irrelevant sensory stimuli in order to facilitate successful attention in performance (Barcelo et al., 2002). Finally, the researchers determined that attentional processing is not just a passive process, but rather is intimately linked

to selection of action that involves multiple processes instantiated by coordinated activity and information flow between many different brain areas (Huda et al., 2018). This research helps to support previous research performed by Ray Guillery. Along with the team of associated researchers, Guillery stated that sensory and motor processing should not be seen as a domain of separate and distinct circuits, but rather as an extensively intermingled network spanning both cerebral and subcortical structures (Guillery et al., 1998). To simplify, incoming sensory signals are transformed as early as possible into explicit motor signals. Further perception and action are then co-determined, and the original sensory inputs lead to perception of task dependant goals and the action is then selected to achieve task demands (Huda et al., 2018).

2.5 Concussion and Relevancy Based Gating

Concussions have been known to influence relevancy-based gating. In a study done by Howell and colleagues (2012) it was determined that there was a disruption in the executive function of concussed adolescents for up to 2-months post injury when compared with healthy age matched subjects. These findings resulted in significantly longer reaction time scores than controls (Howell et al., 2012). In a second study done by Broglio and colleagues (2009), it was found that those reporting at least 3 concussions during their athletic career displayed a fivefold increase in diagnosed mild cognitive impairment and threefold increase in self-reported memory problems compared to non-concussed matched controls. They also found that those with concussion displayed a decrease in the amplitude and increase in latency of the P3a and P3b components, indicating prolonged deficits in the orienting of focal attention, the allocation of attentional resources, and cognitive processing speeds. Along with these deficits, there has also been reporting of a decreased N2 amplitude which indicates a prolonged deficit in attentional systems. Following completion of the study, the researchers discovered that there were specific

deficits in component cognitive processes occurring between stimulus engagement and response execution in the information processing stream. The supressed P3b amplitude in the concussed group may reflect a decreased capacity to allocate attentional resources. On the other hand, the reduced N2 component for the concussed group might reflect a deficit in a general alerting system or the mismatch of a novel stimulus with the mental template or it could also reflect a decrease in cognitive control over response inhibition (Broglio et al., 2009; Broglio et al., 2012; Ferrari et al., 2010).

In a meta-analysis done by Zhang and colleagues (2019), they looked at long-term cognitive performance of retired athletes with sports-related concussions. They discovered that retired male athletes with a self-reported history of concussion may have poor cognition in partial domains. These domains included verbal memory, delay recall, and attention. Other results from the meta-analysis included memory loss in both verbal and recall situations, and hippocampal volume loss. They also found a negative correlation with age and memory. There was a significant decline in memory with increases in age compared to control subjects. Most importantly from this analysis, it was found that when a concussion occurs, the neural network and its mechanisms are disrupted, which leads to a decreased attentional ability and more mechanisms are then needed to compensate for the damaged brain (Zhang et al., 2019). However, this conclusion was made with minimal research and points to a major gap in research involving both concussion and attention, specifically attention with regards to relevancy-based gating and its link to the thalamus and PFC.

2.6 Exercise and Attention

Exercise has a protective physiological effect on multiple organ systems including the cardiovascular, pulmonary, nervous, and neuroendocrine systems. It has been shown throughout

the years that an acute bout of exercise has the potential to modulate cortical excitability, improve cognitive function, cortical processing speeds, the amount of neuroplasticity present, selective attention, short-term memory, aspects of inhibitory control, and the extent of cortical activation (Alves et al., 2014; Singh et al., 2014). Specifically, researchers have been interested in acute moderate bouts of exercise as longer bouts have the tendency to increase hypoglycemia via insulin infusion which can have an adverse effect on cognitive performance (Bullock & Giesbrecht, 2014). It is believed that exercise can decrease the amount of intracortical inhibition present to induce short-term plasticity. The gap seen in this field of research is whether an acute bout of exercise can induce long-term potentiation through factors such as brain derived neurotrophic factor. Popovich and Staines (2015) probed the effects of an acute bout of exercise on ERPs during a tactile discrimination task. It was found that aerobic exercise selectively up-regulated excitability in frontal lobe regions (PFC), thereby promoting greater top-down attentional control during executive function tasks. Specifically, exercise facilitated the sensory gating role of the PFC by suppressing unattended information and amplifying task-relevant information represented in somatosensory evoked potentials (Popovich & Staines, 2015).

In a study done by Alves and colleagues (2014), high intensity training sessions were implemented to determine whether performance could improve performance on a Stroop "Colour Word" task and a Digit Span "Forward" and "Backward" task. They observed an improvement on the Stroop "Colour Word" but not the Digit Span "Forward" and "Backward" task following exercise. A second discovery made was that exercise intensity affects cognitive performance in a U-shaped fashion. This means that moderate-intensity exercise would improve cognition whereas high-intensity exercise would have an adverse effect on cognitive performance (Alves et al., 2014). Another group of researchers followed a similar exercise protocol using EEG analysis

and discovered increases in theta, alpha, and beta spectral band activation, as well, as a high mean frequency in the theta and beta bands in more active or aerobically fit individuals. They also looked at the P3 component and found it to be especially sensitive to changes in physical activity participation and aerobic fitness. There was a larger amplitude and shorter latency found in more fit individuals (Hillman et al., 2008). Thus, the group concluded that physical activity influences baseline electrocortical function and, thus, it may influence cognitive operations (Hillman et al., 2008). To extend this research, it is plausible to suggest that changes in processing due to exercise could have the same effect on the N2, P3 and alpha, theta, and beta bands seen following concussion.

3.0 Rationale

Numerous studies, from both cognitive and neurophysiological perspectives, have suggested that the PFC and thalamus may be particularly susceptible to the forces related to concussion. It has also been suggested in various studies, that concussive effects may persist following the cessation of outward symptomology (Thériault et al., 2009). Recent research has also supported exercise and its effects on attentional correlates (Popovich & Staines, 2015).

Despite these findings, limited research has investigated the effects of exercise and its ability to attenuate ERP changes following symptom resolution in the brain following concussion. A handful of studies in this area suggest that exercise does have the ability to prime attentional correlates (Bullock & Giesbrecht, 2014; Popovich & Staines, 2015). However, this body of work also suffers from several critical limitations. There has been a lack of unity among the structures and functions that are damaged following concussion and exercise has largely been ignored in this context. Furthermore, the potential for the use of exercise in the attenuation of long-lasting changes deserves greater attention, for example, the increase in P3 amplitude and changes in oscillation patterns post-concussion.

This experiment aimed to further identify the effect of exercise on concussive processing to determine if this type of intervention proves useful in preventing the accelerated aging seen in those with a history of concussion. A neurophysiological approach was taken, using EEG to determine whether exercise influences priming of the cortex to optimize neural processing. Here, the N2 and P3 ERPs, as well as ERSPs (theta, alpha, and beta) were of specific interest, given their ties to prefrontal areas and the thalamus, as well as the substantial influence on the allocation of attention given a stimulus. Lastly, EEG was used to determine the magnitude of change between pre- and post-exercise and the direction of change following this type of

intervention. Supplementary data was used as a comparison control for the pre-exercise attentional condition due to limited resources available during COVID-19.

4.0 Objective and hypothesis

The general objective of this experiment is to explore whether exercise can be used as a tool for slowing the accelerated aging seen in the later stages of those with a history of concussion. Briefly, this will be achieved by using an attentional paradigm followed by an exercise intervention to see if the neural correlates of attention can be primed. ERP and ERSP amplitudes and latencies will be compared between non-concussed and previously concussed individuals and a supplementary control group will be used to augment the non-concussed data because of the minimal access to participants due to COVID-19.

Hillman and colleagues (2008) determined that the P3 ERP component was especially sensitive to changes in physical activity participation and aerobic fitness. There was a larger amplitude and shorter latency found in more fit individuals. However, an attentional task was not employed. Based on previous research, it was found that exercise can prime the PFC for greater neural efficiency (Moriarty et al., 2019). Therefore, it is plausible to suggest that following exercise there will be increased P3 and N2 amplitudes compared with pre-exercise conditions in both groups. However, due to the nature of the data and lack of participants, a more exploratory approach will be taken when analyzing and discussing findings.

With regards to the between group comparison, it is hypothesized that following exercise the concussed group will have a larger increase in P3 and N2 amplitudes, as comparatively, there is greater depression in P3 and N2 baselines following concussion (DeBeaumont et al., 2007). This means a lower starting point for concussed verses non-concussed individuals. Contrastingly, the changes in ERSP data seen previously post-concussion are mixed and no real consensus has been made. Because of this uncertainty of post-concussive restructuring to ERSPs an exploratory

approach will be taken, again, supplementing with outside data to mimic the pre-exercise non-concussed attentional paradigm that was employed.

Lastly, based on previous research (Hillman et al., 2008) it is hypothesized that there will be no differences in either accuracy or response time between the groups, or following exercise, with regards to target recognition or delayed recall of images. Although there are changes in ERP patterns following concussion, there have been no proven behaviour changes six months post-concussion if all symptoms have ceased.

4.1 Exploratory Objective and Hypothesis

Previous research has not yet identified if exercise has the ability to alter the neural correlates of attention following concussion. Therefore, an exercise intervention will be employed. If significant differences emerge, it is hypothesized that P3 and N2 amplitudes will be larger following exercise in both groups. Further, it is hypothesized that the magnitude of change will be larger in the concussed group as compared to the non-concussed group.

With regards to the concussed group, attention disruptions and reaction times will be looked at on a case-by-case basis, comparing individual data to both a studied and supplementary norm.

5.0 Methods

5.1 Participants

Participants in this study comprised 2 groups: a non-concussed group and a previously concussed group (greater than 6 months post-concussion). A total of 8 participants were recruited, 6 non-concussed and 2 concussed (3 female, 5 male). Inclusion criteria for the previously concussed group requires that at least 6 months prior they had suffered a concussion. The concussed group sustained at least one medically diagnosed concussion and were clinically cleared to return to both cognitive and physical activity. Apart from being concussed, the participants were free from any additional peripheral or central nervous system injuries. The non-concussed group did not sustain, and were not suspected to have sustained, a previous concussion and similarly were free from any additional deficits to the nervous system. All subjects were required to be within the ages of 21 and 30, achieved at least a moderate level of activity as determined by the International Physical Activity Questionnaire (IPAQ), and be fluent in English. Subjects were excluded from the study if at any time during testing there was return of symptomology. All subjects were free from neurological disorders, medication that alters the central nervous system, and any substance abuse. Fluency in English was necessary to ensure complete understanding of the instructions and accurate data collection. Subjects were recruited by word of mouth, and posters placed in various locations on campus, and were from both within and outside of the University of Waterloo.

5.1.1 Demographics. Subjects completed a combination of standardized forms, as set out by Broglio and colleagues (2018) in the concussion common data elements. Forms that each participant filled out included personal medical history, participants family psychological history, migraine history, substance use, and concussion history. Along with the concussion common data elements, the IPAQ was completed to determine activity level prior to exercising.

The Get Active Questionnaire (GAQ) was completed to determine readiness and ability to participate in exercise. Finally, those participants who regularly participated in sport filled out an additional injury report from the common concussion data elements (Broglio et al., 2018). Additionally, participants completed the Stanford Sleepiness Scale (SSS) just prior to testing to determine level of alertness.

5.2 Experimental Design

Prior to testing, participants completed a Trail Making Test (TMT) in order to determine homogeneity among participants' cognitive capabilities (Broglio et al., 2018). To measure the capability of participants' attentional systems, a protocol based on Yamaguchi et al., (2004), was employed. Standard (70% or 73%) and target (20%) stimuli were represented by a white triangle drawing presented on a black background. The target was an inverted standard stimulus. Novel stimuli (10% or 7%) consisted of 150 images chosen from the International Affective picture System (IAPS). Highly emotional stimuli such as those showing an injured body part were excluded and images were selected based on easily recognizable objects within the image. Each image was presented in the center of the screen at a size of 770x1030 pixels. The duration of each stimulus was 75 ms. The interstimulus interval (ISI) between all images was 500 ms.

A custom LabView (National Instruments, Austin, Texas, USA) program was used to generate the image randomization across blocks. In each block, 30 images (6 target, 21-22 standard, and 2-3 images from IAPS) were shown, of which only the target stimuli required a response. The response was the squeeze of a bulb that was held in the participant's right hand. In total, 600 images were shown over 30 blocks, all of which were created prior to testing such that each subject received the same randomized blocks. After each of the blocks were completed, participants were asked 2 questions: 'How many pictures did you see?' (The answer could only

be 2 or 3) and ‘Can you recall what the pictures were?’ Participants did not have to recall pictures in sequential order.

All subjects underwent an exercise intervention following the first set of blocks. During the exercise session participants cycled on an electric cycle ergometer. They started with a 5-minute warm up at 25 Watts, followed by a 20-minute bout of acute exercise at 70% of heart rate max (220-age). The wattage was increased by intervals of 25 every minute following the warmup, until 75% of max heart rate was reached. The intervention was completed with a 5-minute cool down at 25 Watts. Heart rate (HR) was monitored every minute using a polar heart rate monitor and rate of perceived exertion (RPE) was measured every 5 minutes using the Borg scale. Pedalling rate was maintained between 50 and 70 revolutions per minute to ensure mechanical efficiency across participants. Exercise was terminated immediately if concussive symptoms arose. Following completion of the intervention participants rested for 10 minutes and heart rate was recorded at 5 and 10 minutes following the cessation of exercise, upon which, another different 30 randomized block trials was completed.

5.3 Data acquisition

EEG was collected during the block trials using a 32-channel cap (Quik-cap, Compumedics Neuroscan, NC, USA), with the main electrodes of interest being Fz, Cz, CPZ, and Pz (according to the International 10-20 system). Electrodes were referenced to linked mastoids, with all channel impedances less than 5 kΩ. The data was digitized at 1000 Hz and low-pass filtered at 200 Hz (SynAmps^2 Compumedics Neuroscan, NC, USA).

In addition to the electrophysiological data, behavioural data was also collected during the target and novel portion of the oddball paradigm. Participants’ response time and accuracy was acquired via a custom LabView program (National instruments, Austin, Texas, USA), which

recorded the participants' response time to target stimuli, as well as, 'misses' and 'false alarms'. Novel stimuli recall (both # and image) was recorded following the end of each of the 30 blocks.

5.4 Data analysis

EEG data was analyzed using EEGLab (Swartz Center for Computational Neuroscience, CA, USA) software. All continuous data files were epoched from -100 to 700 ms of each stimulus type. All epochs were manually inspected for noise and artifacts that may have been produced by outside generators; either biological or non-biological sources. Epochs were then averaged within each stimulus type (Target, Non-target, Novel) before extracting the values of interest. Event related spectral changes were explored to further investigate EEG changes following concussion, such as, alpha, theta, and beta frequency band enhancement. Based on previous research (Drollette et al., 2014; Herrmann & Knight, 2001; Hillman et al., 2009; Kumar et al., 2005; Ligeza et al., 2018; Polich & Lardon, 1997; Yamaguchi & Knight, 1990), the amplitudes for each of the potentials of interest were determined as follows:

	Novel	Target - Non-Target
Theta	200-460	225-410
Alpha	200-460	260-435
Beta	195-355	250-470

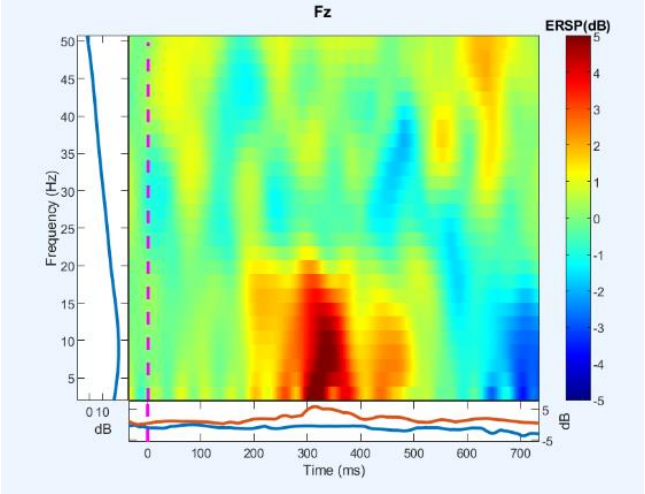

Figure 1 *- ERSP Analysis: Time points for latency extraction in target/non-target and novel stimuli visually taken from ERSP plots. ERSPs were taken from -100ms pre-stimulus to 700ms post-stimulus. Target and non-target plots were visually inspected for spectral changes and averaged to determine temporal intervals. Novel stimulus plots were visually inspected and averaged to determine temporal intervals.*

- N2: greatest negativity between 250-500 ms from Fz and Pz (Figure 2)
- P3: greatest positivity between 250-650 ms Fz and Pz (Figure 3)
- Theta band: 4-8 Hz

- Alpha band: 8-12 Hz
- Beta band: 12-35 Hz

Participant behavioural data was analyzed using a custom LabView (National Instruments, Austin, Texas, USA) program. For each block, number of targets hit as well as misses and false alarms were determined. Response time was determined from the time the target stimulus was displayed to the time the bulb was squeezed. Response times were averaged over the 30 blocks before and after exercise.

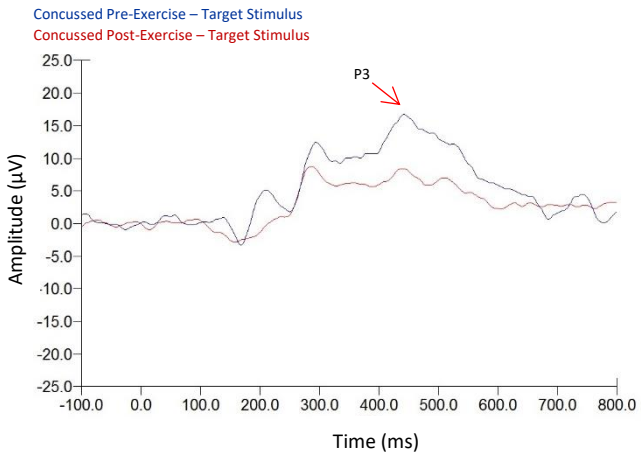

Figure 2 *- P3 Target Stimuli Concussed:* P3 wave lengths were epoched 100 ms pre-stimulus to 700 ms post stimulus and epochs were averages across all target stimuli.

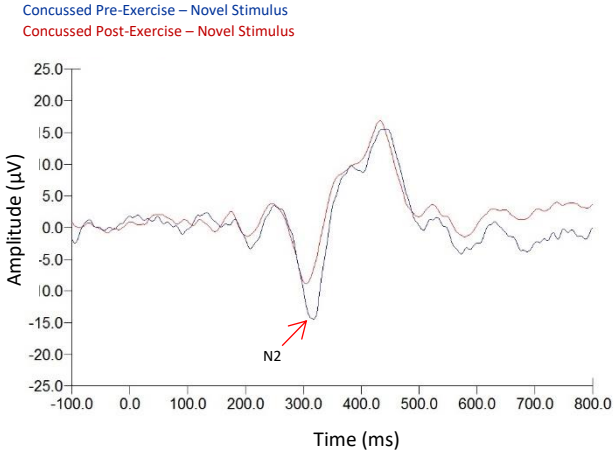

Figure 3 *- N2 Novel Stimuli Concussed:* N2 wave lengths were epoched 100 ms pre-stimulus to 700 ms post-stimulus presentation and epochs were averaged across all novel stimuli.

5.5 Statistical analysis

The P3 (specifically the P3b) is maximal parietally and because of this amplitudes and latencies were taken from Pz electrode cites during target stimulus presentation. Conversely, because the N2 is more fronto-centrally located, amplitudes and latencies were taken from Fz electrode cites during novel stimulus presentation. All dependant measures for the non-concussed group (P3/N2 amplitudes and latency, theta, alpha, and beta band synchronization/desynchronization, accuracy and response time for targets, and accuracy for

image recall) were put through a 2-tailed t-test to compare pre and post exercise. The concussed participants (001 & 006) data was visually inspected to determine over arching latency trends and then compared to non-concussed controls (Figure 1). Lastly, to directly test this hypothesis the non-concussed group and supplementary data from Guo et al., (2019) (for P3 data), sample data (for N2), and ERSP averages from Adams (2020), will be used to determine a 95% confidence interval pre-exercise through which the two single concussed cases will be compared to determine whether they fall within the interval both pre and post exercise.

6.0 Results

6.1 Participant Characteristics

A total of 8 participants were recruited for this experiment, 6 participants in the non-concussion group (NC) and 2 participants in the concussion group (C) (Table 1). Of the total 8 participants, 4 were female and 4 were male (NC 4F, 2M; C 2M). The participants' ages ranged from 21-30 and the average age was 25.13 ± 4.16 (± standard deviation). All participants completed the GAQ and were cleared to participate in exercise. From the IPAQ all participants except one from the NC group were categorized as highly physically active. This classification equates to vigorous-intensity exercise on at least 3 days/week OR 7 or more days consecutively of walking, moderate to vigorous intensity exercise amassing at minimum 3000 MET-minutes/week. The single participant from the NC group was categorized as being moderately physically active. This classification equates to 3 or more days of vigorous exercise at 20 minutes or more/day OR 5 or more days of moderate intensity exercise and/or walking at minimum 30 minutes/day OR 5 or more days of a combination of the activities mentioned above achieving a minimum of 600 MET-minutes/week. It was required that all participants recorded at least a moderate level on the IPAQ to be included in the study. All participants were free from neurological disorder and substance abuse as determined by the Concussion Common Data Elements (Broglio et al., 2018). Participants in the NC group reported not sustaining a clinically diagnosed concussion and, similarly, reported not participating in any contact sports throughout their lives.

Participants from the concussion group are broken down into their individual cases in order to further understand the electrophysiological results. Participants 001, age 30, reported sustaining 3 clinically diagnosed concussion, each of which were sustained playing football in high school at age 13, 15 and 17. Each of the concussions resulted in a loss of consciousness

(LOC) for 5 seconds, 10 minutes, and 5 seconds, respectively. During the second concussion (age 15), this participant reported having difficulty remembering for 1-hour post-concussion. Lastly, symptomology lasted a total of 10, 45 and 2 days for each consecutive concussion. Other characteristics that participant 001 reported was a familial migraine disorder and learning disability (dyslexia).

Participant 006, age 26, reported sustaining 7 concussions that they could recall but also reported withholding symptoms from clinicians and trainers following suspected subsequent concussions. This may mean there were other injuries or subconcussive traumas that were unreported. This participant described a career in both hockey and football as an aggressive player. Injuries were received in both contact during play and fights during the season. Concussions were received at age 14, 2 at age 16, 17, 18, 21, and 22, however, the only concussion that resulted in a LOC was at age 16 and the time spent unconscious is unknown. This participant reported having difficulty remembering in the first 2 of their concussions but for only 5 minutes per. Symptomology was greatest during the first 2 concussion at 14 and 30 days respectively, and all subsequent concussion symptomology ranged from 1-3 days. Another disorder that this participant reported was clinically diagnosed depression at age 25.

Participant Characteristics					
Participant	Group	Gender	Age	IPAQ Category	Migraine History
001	C	M	30	HIGH	Y
002	NC	F	26	HIGH	N
003	NC	M	23	HIGH	N
004	NC	F	23	HIGH	N
006	C	M	26	HIGH	Y
007	NC	F	21	MODERATE	N
008	NC	M	21	HIGH	N
009	NC	F	22	HIGH	N

Table 1 - Participant Characteristics

6.2 Supplementary Data

On the SSS participants were asked to rate their degree of sleepiness on a scale of 1-7. Participants' scores ranged from 1-3, except for 1 participant who reported a 4 prior to the experiment (1 = feeling active, vital, alert, or wide awake; 2 = functioning at high levels, but not at peak; able to concentrate; 3 = awake, but relaxed, responsive but not fully alert; 4 = somewhat foggy, let down). The mean of the SSS was 2.5 ± 1. Statistical analyses were not carried out on this data.

Participants also completed the Trail Making Test to determine cognitive competency across groups. Two participants were excluded from this data as they did not complete this test prior to experimentation. On part A of the TMT, participants in the NC group finished in an average of 19.42 seconds ± 3.8, whereas participants 001 and 006 finished in 21.98 and 12.56 seconds, respectively. Part B of the TMT revealed an average of 47.86 seconds ± 8.36 for the NC group and 37.31 and 31 seconds for participants 001 and 006. Concussion participants either fell within one standard deviation or below 1 SD on all scores. No statistical analyses were carried out on this data.

6.3 Exercise Data

The NC group had an average resting HR of 72 ± 10.3 bpm and the C group had a resting HR of 53 and 56 for 001 and 006, respectively. The average target HR (70% of HR max) for NC was 137.83 ± 1.86 bpm and 134 and 135 bpm for 001 and 006. Lastly, the average HR during the 20-minute exercise session for NC was 137.01 ± 4.08 and 135.3 and 135.25 for 001 and 006. During the exercise session, all participants reached 70% of their HR max. The average RPE score as determined by the Borg scale was 12.47 ± 1.5 for NC and 12.4 (001) and 11 (006). Following the first 5 minutes post-exercise the average HR for NC was 101.3 ± 11.72 and was

63 for 001 and 94 for 006. Following 10 minutes of rest post-exercise, average HRs were 86.5 ± 10.45 for NC and 58 and 82 for 001 and 006, respectively.

HR and RPE							
Participant	Group	Resting HR	Target HR	Session AVG	AVG RPE	HR 5mins Post	HR 10min Post
001	C	53	134	133.35	12.4	63	53
002	NC	77	135	132.2	13	96	71
003	NC	87	138	134.55	12.2	115	93
004	NC	78	138	143.1	9.9	114	102
006	C	56	135	135.25	11	94	82
007	NC	64	139	134.1	13.6	107	86
008	NC	66	139	138.9	12.8	89	85
009	NC	60	138	139.2	13.6	90	82

Table 2 - Heart rate and Rate of Perceived Exertion

6.4 Behavioural Data

The average reaction time (RT) for the NC group prior to exercise was 505.66 ± 118.08, 499.221 ± 93.76 for 001 and 479.033 ± 99.105 for 006. Following exercise, average reaction times were 507.798 ± 120.2, 486.411 ± 89.306, and 459.267 ± 102.332, respectively. A t-test pre- and post-exercise for NC revealed no statistical significance ($t_5 = -0.37$, $p = 0.72$). All RTs for the C group were lower than the mean or fell within 1 SD. Accuracy was scored out of 180 possible targets. The average percentage accuracy for NC was 98.2% pre- and 98.3% post-exercise, 001 had 100% accuracy pre- and post-exercise, and 006 had 98.9% pre- and 97.2% accuracy post-exercise. The average number of 'false alarms' hit was 10.176, 6 and 1 pre-exercise, and 11, 1 and 4 post-exercise for NC, 001, and 006, respectively. The t-test revealed no statistical significance between pre- and post- exercise for NC ($t_5 = -0.18$, $p = 0.87$). On all trials the concussion group hit a lower number of false alarms both pre- and post-exercise than the NC group.

Pre-exercise, the NC group was 98.6% accurate, post-exercise they were 99% accurate for recall of the number of images. Both 001 and 006 were 100% accurate pre-exercise, post-exercise 001 was 100% accurate and 006 was 98.6% accurate. For the recall of what the images were, NC was 98.6% accurate pre- and 95.8% accurate post-exercise. Participants 001 and 006 were both 100% accurate pre-exercise, however, post exercise 001 was 97.2% accurate and 006 was 93% accurate. In general, participants were less accurate following exercise. However, participants that had sustained a concussion were on average, more accurate than their non-concussed counter parts. This may be due in part, to the lack of participants in the C group.

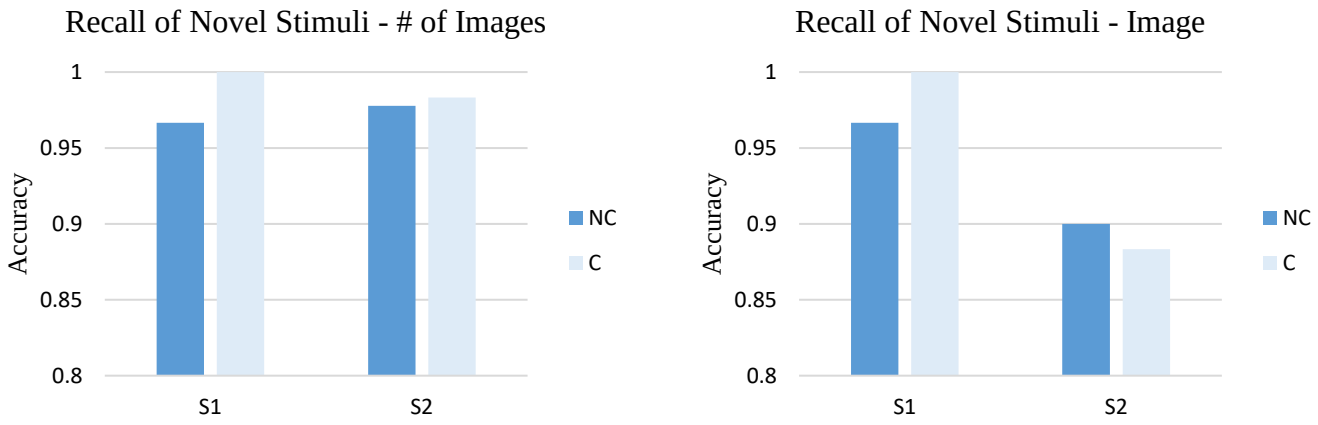

Figure 4 - Recall of Novel Stimuli, both number of images and what the images were. Percent accuracy was recorded out of 73 images for pre-exercise and 72 images for post-exercise. A higher score is representative of a better performance on recall.

6.5 ERP Amplitude Analysis

6.5.1 P3

A paired sample t-test on P3 ERP data pre- and post-exercise in the NC group revealed no significant difference between time points. Again, in all electrode sites, across all time points, there was no statistical significance found because of the nature and lack of participant data due to COVID-19. A sample set of data will be used to discuss trends across groups and time points. The 6 NC participants collected in this study were compared to a sample (S) mean. A 95%

confidence interval (95% CI) of the sample mean was used to determine C group similarity pre- and post-exercise. Pre-exercise, the NC group, because of the large variation in baseline amplitudes and large standard errors (SE), was found to be similar to that of the sample mean (NC AVG = 7.38, SE = 4.05; S AVG = 8.402, 95% CI = 1.81). Participant 001 pre-exercise had a larger P3 amplitude in the Pz electrode by 9.46 µV, compared to the sample mean, falling outside of the 95% CI. Participant 006 also had a larger amplitude pre-exercise, 5.39 µV higher,

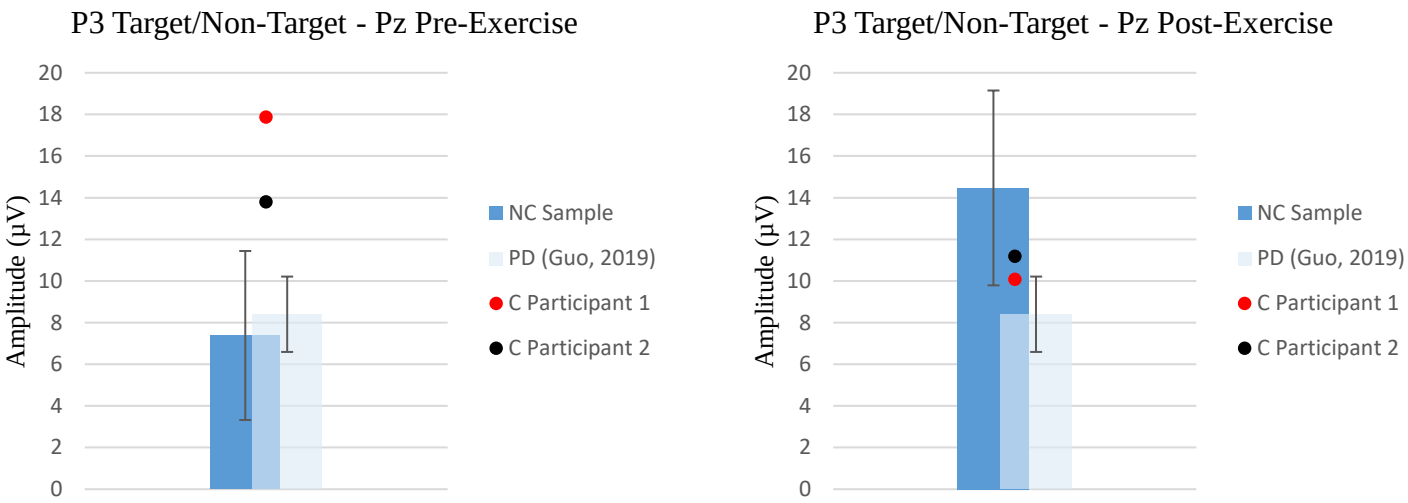

Figure 5 *- P3 Target/Non-Target Pre- and Post-Exercise:* Standard errors (SE) are represented on the non-concussed (NC) group (n=6). The 95% CI is represented on the population data (PD) (n=21). Concussion data was represented with respect to the 95% CI on the population data pre- and post-exercise. Red represents the first concussed participant and black represents the second concussed participant.

also falling outside of the 95% CI. Following exercise, the NC group was found to be similar to that of the sample mean (NC AVG = 14.47, SE = 4.68; S AVG = 8.40, 95% CI = 1.81). A paired t-test revealed no statistical difference in the Pz electrode pre- to post-exercise in the NC group (t_5 = -1.12, p = 0.29). The amplitude of P3 wave following exercise was depressed in participant 001. Post-exercise the P3 amplitude fell within the 95% CI of the sample mean. Meaning, participant 001, was similar to the NC and sample baselines post-exercise. Participant 006 on the other hand, had a lower amplitude pre-exercise (M=13.79), but still fell outside of the 95% CI. Following exercise, the P3 amplitude decreased (M=11.18) and fell just outside of the 95% CI.

The trend was similar to that of participant 001 and was closer to the NC and sample baselines, post-exercise.

6.5.2 N2

A paired samples t-test on N2 ERP data pre- and post- exercise in the NC group revealed no significant difference between time points in the Fz electrode ($t_9 = 0.21$, $p = 0.84$). Quite understandably due to circumstances out of our control, no measures following the t-test reached statistical significance in any of the electrodes tested. Trends will be further discussed with regards to a sample set of data. Due to the variability in the NC group data, both the pre-and post-exercise conditions were found to be similar to that of the sample data. Following exercise, the N2 amplitude in the NC group increased (Pre- M = -17.97±6.67; Post- M = -19.44±15.95). This trend matches that of previous literature saying that P3 and N2 amplitudes are increased following moderate intensity exercise. Participant 001 decreased in amplitude following exercise

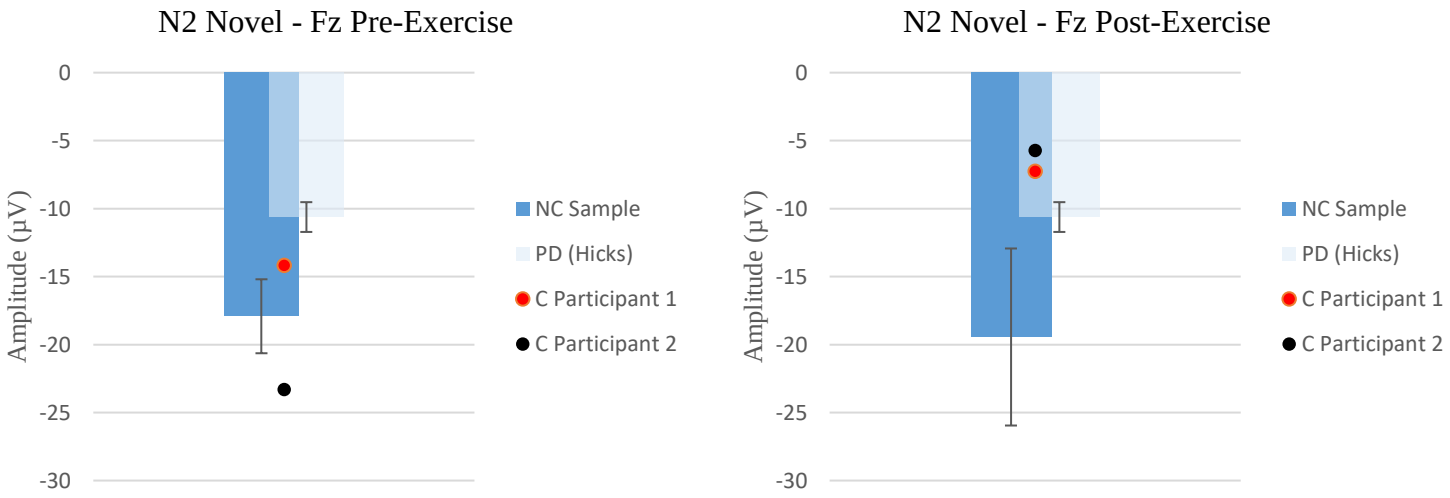

Figure 6 *- N2 Novel Pre- and Post-Exercise:* Standard errors (SE) are represented on the non-concussed (NC) group (n=6). The 95% CI is represented on the population data (PD) (n=13). Concussion data was represented with respect to the 95% CI on the population data pre- and post-exercise. The first concussed (C) participant is represented by red and the second concussed (C) participant is represented by black.

from -14.174 µV to -7.243 µV. Although the mean following exercise does not fall within the 95% CI, the trend is similar to that of the P3. The post-exercise condition amplitude trends

towards the baseline amplitudes of the sample condition but moves in the opposite direction of the NC group following exercise. Participant 006 has a similar trend to participant 001 but had a greater decrease pre- to post-exercise (Pre- M=-23.36; Post- M=-5.79).

6.6 ERP/ERSP Latency Analysis

Latencies for ERSP power analyses were taken from visual inspection of the plots and averaged across novel stimuli and target/non-target stimuli and, because of the nature of these values, trends will be discussed. Latencies were as follows: 200-460ms, 195-355ms, and 200-460ms for novel stimuli in theta, alpha, and beta bands, respectively. This corresponds to the latencies from ERP amplitudes calculated for N2 amplitudes also drawn from novel stimuli. In the NC group latencies for N2 were 270.3±49.11ms pre-exercise and 236.3±18.74ms post-exercise. For the C group, latencies were determined as follows, 252ms and 167ms for pre- and post-exercise. P3 amplitudes, notably, have later latencies as they are parietally maximal. ERSP amplitudes were as follows: 225-410, 250-470, and 260-435 for target and non-target stimuli in theta, alpha, and beta power bands, respectively. Correspondingly, P3 target amplitudes in the NC group were 456.8±64.24ms pre- and 457.3±87.64 post-exercise. The C group pre-exercise had a latency of 499.5ms and a post-exercise latency of 393.5ms. The similarity in latencies in both ERSP and ERP analyses may be representative of a relationship between cortical oscillations and attentional changes in P3 and N2 amplitudes following exercise and concussion.

6.7 ERSP Analysis

6.7.1 Target & Non-Target

Following ERSP analysis, non-target amplitudes were subtracted from target amplitudes to determine amplitude changes pre- and post-exercise. Using data from Adams et al., 2020, comparisons were made pre-exercise for the ERSP means in both the C and NC groups (Figure

7). In the theta band, controls from the supplementary data displayed an amplitude of 0.61 dB compared to the NC which was 0.81 dB. The alpha band was also comparable at 0.55 dB and 0.81 for the supplementary data and NC group, respectively. Similarly, the supplementary data for the concussed group resembled our own data. Levels were lower compared to the NC group pre-exercise. Beta bands were almost zero in the supplementary data however and will not be examined further.

The NC group revealed an overall decrease in theta, alpha, and beta band synchronization in both Fz and Pz electrodes (Figure 8). However, the greatest decrease in synchronization is seen more parietally in the theta and alpha bands (Figure 7). Power in the theta band decreased from 0.9 dB to 0.23 dB pre- and post-exercise and in the alpha band from 0.72 dB to 0.18 dB. There was a decrease frontally, and not just to the extent of the parietal sites. Paired t-tests revealed no significant effect over time from pre- to post-exercise. The C group on the other hand had differential results frontally and parietally. In Fz electrode site both participants 001 and 006 had a large increase in synchronization. Participant 001, in theta and alpha bands had a 0.49 dB and 0.95 dB increase in synchronization from pre- to post-exercise. Whereas participant 006 had a 0.9 dB and 0.61 dB increase in theta and alpha band synchronization from pre- to post-exercise. Differentially in the parietal sites, participant 006 showed trends similar to the NC group, in which synchronization was decreased following exercise. Participant 001, however, showed desynchronization across all bands.

6.7.2 Novel

Novel stimuli, unsurprisingly, had larger amplitudes overall due to the novelty and saliency of the stimuli being displayed. Because of the frontal nature of the novel stimuli representation, ERSP amplitudes were taken from electrode site Fz. The general trend in

target/non-target ERSPs showed decreases in synchronization, and similarly so did the novel ERSPs. The NC group pre-exercise showed synchronization in the alpha (3.95 dB), theta (2.81 dB), and beta (0.02 dB) bands. Post-exercise there was a decrease in synchronization in both the alpha and theta bands, but a small increase in synchronization in the beta band. Similarly, participant 001 showed a general trend of desynchronization. Each of the bands saw decreases post-exercise, 1.06 dB, 1.02 dB, and 0.28 dB in theta, alpha, and beta bands, respectively. Similarly, participant 006 showed a decrease in synchronization in both theta and alpha bands but a change from synchronization to desynchronization in the beta band.

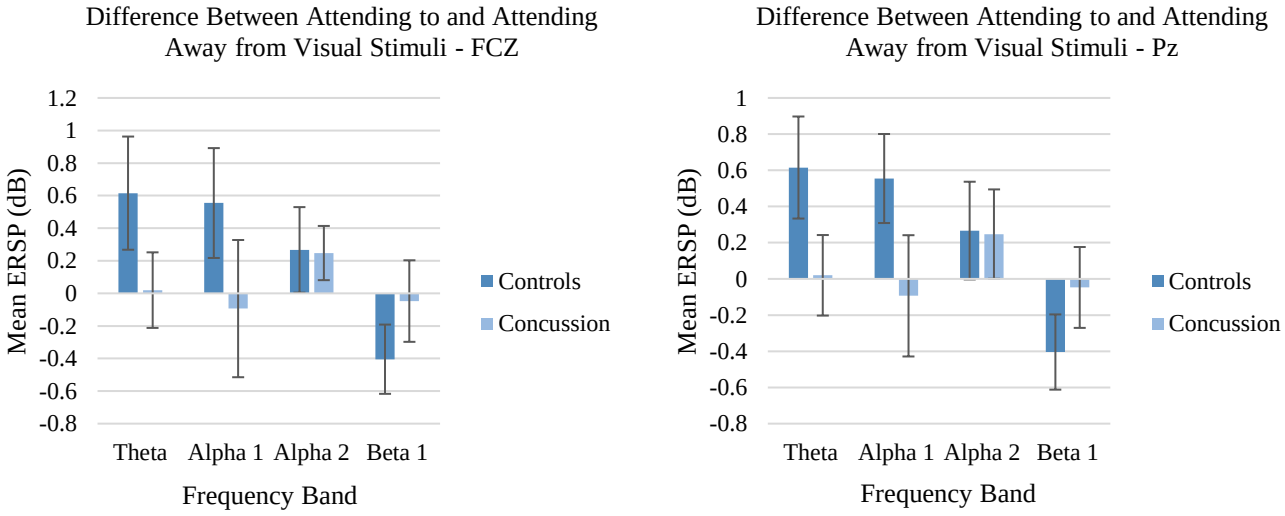

Figure 7 - Supplementary Data for ERSP Analysis (Adams et al., 2020): Data used for comparison of concussion and NC comparison pre-exercise. Trends were examined to examine validity of the results collected. Error bars represent standard error (SE).

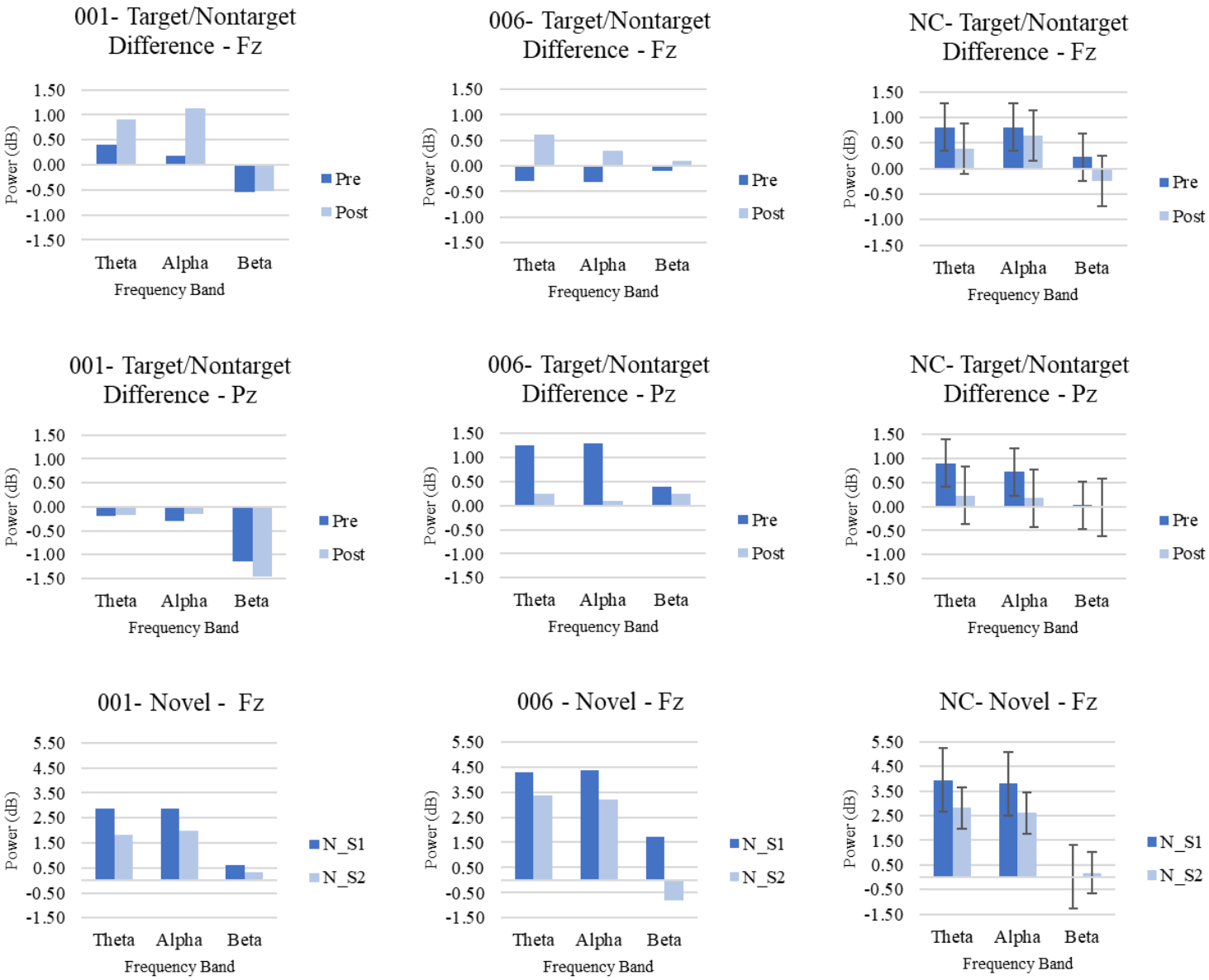

Figure 8 - ERSP Power Analysis - Theta, Alpha, Beta: The graphs are representative of peak power during stimulus presentation. Non-targets were subtracted from targets to represent power changes pre- and post-exercise in electrodes Fz and Pz. Novel stimuli were extracted from Pz electrodes. Error bars on NC groups represent SE.

7.0 Discussion

The results of our study are generally consistent with previous literature outlining how exercise augments attentional correlates, suggesting that exercise may in part change the deficits seen in concussed individuals (Alves et al., 2014; Hillman et al., 2008; Popovich & Staines, 2015; Singh et al., 2014). However, incongruent with previous literature, concussed participants showed differential results from preceding data. Our results add to the literature in the following ways. First, concussed participants were studied on a case-by case basis. Therefore, results from these participants allowed us to view neurophysiological changes with respect to a specific concussion history. Second, we attempted to draw conclusion on long-term changes following concussion and the possibility of exercise as a long-term solution to the accelerated aging process observed later in life. Our results provide, in part, some insight into the relationship between the concussed brain and exercise as a long-term intervention.

The main objective of our study was to examine exercise as a tool to slow the accelerated aging process which is presently of broad and current interest in the neuroscience community. Though our results are exploratory in nature, they do to some extent support the notion that exercise throughout life, after experiencing a concussion, can change the neural correlates of attention. Following exercise, the concussion group's P3 and N2 amplitudes resembled that of our control group. Latencies were also similar across NC and C groups. It was hypothesized that exercise would increase the P3 and N2 amplitudes in both the NC and C groups. Following exercise, in both the P3 and N2 wave forms, the NC group displayed an increase in amplitude. However, the C group did not support this hypothesis. It was predicted that pre-exercise the C group would have depressed amplitudes in the P3 and N2 waveforms (DeBeaumont et al., 2007; Guay et al., 2018; Theiriault et al., 2009), but this was not the case. Prior to exercise, the C group

had elevated amplitudes compared to the NC group in both the P3 and N2. Following exercise, unlike the NC group, the C group decreased in amplitude such that their amplitudes were similar to the sample group's baselines. Participant 001 following exercise fell within the 95% CI and participant 006 fell just outside of this interval following target stimuli presentation. Following novel stimuli presentation post-exercise, it was predicted that following exercise the C group would see a greater increase in amplitudes compared to the NC group because of the depression that has been seen in previous literature. As stated above, there was no depression seen in amplitudes, however, the C group did have a greater change in P3 and N2 waveforms following concussion, just not in the direction that had been predicted. Greater decreases were seen overall, in both concussion participants' post-exercise. Lastly, it was predicted that there would be no differences in IAPS image recall, accuracy or response time in the C group compared to the NC group. This was the case, as the C group had similar accuracy and response times, falling within 1 SD of the NC mean, supporting previous literature that reported comparable behavioural characteristics. (e.g., accuracy and response time) (Hillman et al., 2008).

ERSP, being mainly exploratory due to the lack of consensus among other researchers (Munia et al., 2017; Barlow et al., 2018), showed evidence of oscillatory change following exercise. Sample data from Adams allowed the comparison of pre-exercise concussion data in order to determine if our baseline levels were similar to that of a larger sample (Adams et al., 2020). Pre-exercise, the NC group was comparable to the sample data and matched general trends. In the frontal and parietal sites, participant 001 showed the same general trends as the concussed group from the sample data pre-exercise. Participant 006 was similar at frontal sites displaying either low synchronization or desynchronization. Dissimilarly, in parietal sites participant 006 showed a much higher synchronization than both the NC group and the controls.

Because of the difference in stimuli to our own data, no statistical comparison was made; only trends were observed. Target data from our study was compared to 'attending to' conditions in Adam's data, and non-target data was compared to the 'attending away' conditions from the control data (Adams et al., 2020). The parallels seen in our data and the control data allow us to make inferences about the changes post-exercise in the concussed group compared to the NC group. Post-exercise the NC group saw decreases in theta, alpha, and beta synchronization for target/non-target stimuli. Conversely, there were increases in synchronization across all bands pre- to post-exercise in participant 001 in Fz. In Pz there was a decrease in desynchronization in theta and alpha bands, but an increase in beta. Participant 006 mimicked the NC group in parietal sites, but in frontal sites matched that of participant 001. With regards to the novel stimuli, all groups (NC, 001, 006) had a decrease in synchronization following exercise.

7.1 Participant Characteristics

Both groups had similar descriptive characteristics. Resting HR and IPAQ results gave some indication that groups were comparable. The concussion history of the participants was unsurprisingly, where differences were seen in the characteristics of the participants. Non-concussed participants were free from any clinically diagnosed concussion and did not participate in any contact sports throughout life. Participant 001 had sustained 3 clinically diagnosed concussions, all resulting in a LOC, with time spans of unconsciousness rangeing from 5 sec-10 min. Symptomology ranged from 2-45 days and there was report of difficulty remembering in all 3 concussions. Participant 006 reported sustaining 7 concussions and only 1 resulted in a LOC. This participant had difficulty remembering directly following the insult in 2 of the 7 concussions and symptomology ranged from 1-30 days post-concussion. It may also be important to report that this participant was later diagnosed with clinical depression.

7.2 Exercise Data

During the exercise portion of our study, participants were required to complete a 20-minute bout of moderate intensity exercise on a recumbent bike. The average percentage of HR max reached during exercise for each group was within the range set prior to exercise. The range of RPEs loosely tied to moderate intensity exercise is 12 to 14. Our participants fell on the low end of this range. However, because of the maintenance at the HR range required, we are certain that a moderate intensity level was reach among participants. All participants remained within the set RPM range, so we are confident that this variable was controlled for. Standard deviations were higher in both the 5- and 10-minutes post exercise, which reflects the variability in times taken to go down from person to person and may also reflect fitness level across participants.

7.3 Neurophysiological Data

Generally, damage following concussion is masked by the ability to perform behaviourally at the same level as non-concussed counterparts (Guay et al., 2018). The response time, accuracy and recall results present in our study supports previous literature stating that there are no behavioural changes seen after symptom resolution following concussion (Guay et al., 2018). These results support the idea of cognitive reserve. Following concussion, increases in functional connectivity, especially in the frontal regions, are commonly seen, even in the years following symptom resolution. At first glance, the ERP changes displayed in our results depict an increased need for cognitive resource allocation as the P3 is increase following target stimulus presentation, however, the lack of behavioural changes suggest that those with concussions recruit alternate pathways (resources from other sensory modalities) in order to maintain behavioural goals. Task performance under this assumption will only decrease when increases in

activation in certain networks and recruiting of alternative neural resources limits are reached (van Dinteren et al., 2014).

7.3.1 P3 and Target/Non-target Stimuli

The main hypothesis for the objective of this study was not supported, as our C participants did not have an increase in amplitude in P3 nor N2 following exercise. In fact, our pre-exercise results showed an increased amplitude from the baseline levels seen in the NC. In most other literature there has been a trend seen of depressed P3 and N2 amplitudes following concussion (DeBeaumont et al., 2007; Guay et al., 2018; Theiriault et al., 2009).

The P3 waveform is a conscious updating process involved in cognitive processing. A possibility for the difference in P3 amplitudes between NC and C groups may be due to a lack of filtering of incoming information following concussion which puts more demands on attentional resources. Because the P3 is indicative of stimulus processing and is an index for the amount of cognitive resources allocated to a given task (van Dinteren et al., 2014), the heightened amplitude in our concussed group may represent issues in attentional allocation following target stimulus presentation. That is, there may be an inability to select appropriate and targeted sensory streams. Therefore, increased mental effort is devoted to a particular task (van Dinteren et al., 2014). Conversely, information may not be filtered during stimulus presentation and this is why we seen an increase in P3 amplitude in the pre-exercise conditions in both concussion participants. Meaning more information unrelated to task demands is processed, increasing the P3. These processes are largely subserved by the thalamus in filtering and routing incoming information across multiple brain regions. The thalamus itself has recently been thought to be a prime area for long-term damage following concussion and because of this may represent the changes seen in our study (Grossman & Inglese, 2016; Shin et al., 2014). Torsional forces could

produce fluid waves that traverse through the lateral ventricles and could conceivably reach and injure deeper cortical structures, including the thalamus (Shin et al., 2014). Theoretically if the thalamus serves to control functional connectivity across the brain, damage in this area might affect connectivity to the DMN and other brain regions responsible for attention. Due to the uncertainty among researchers as to the exact components that are responsible for the P3 presentation (Ledwidge & Molfese, 2016; Rugg et al., 1988; Rusinak et al., 2013), it is plausible to suggest that there are separate mechanisms behind the changes seen in both the NC and C group, being that their network patterns are likely different due to post-concussive damage or adaptation in the attentional network.

7.3.2 N2 and Novel Stimuli

In contrast, the N2 wave form is weighted heavily in the frontal region of the brain and is related largely to the novelty of a stimulus and the engagement of various attentional systems (Ledwidge & Molfese, 2016; Rugg et al., 1988). Our results suggest that there is increased cognitive demand following the novel stimuli in the concussion group, representing an inability to categorize incoming stimuli succinctly. The N2 represents the mismatch between the current stimulus relevant to the behavioural goals and the mental template created to promote task demands (Ferrari et al., 2010). The N2 is only decreased when there is heightened perceptual fluency in which active memory representations contribute in a top-down fashion, to the perceptual processing of the current stimulus (Ferrari et al., 2012). Increased cognitive demand following novel stimulus presentation could be a result of an increase in neural network connectivity seen frontally, post-concussion. These increases are thought to be present to compensate for decreases in processing efficiency in the same networks (van Dinteren et al., 2014). Previous literature has suggested that the PFC is a prime candidate for concussive damage

(Talavage et al., 2014), and as such represents the increases in neural resources that are allocated to attentional tasks in order to compensate for the frontal region damage. It is then plausible to suggest that the increase in N2 amplitude following concussion is a result of an early processing stream issue.

Following exercise, it was hypothesized that the C group would have a larger increase in amplitude in both the P3 and N2 than the NC group, such that the C data would resemble that of the NC data pre-exercise. Our data only displayed this hypothesis in part. Pre-exercise our concussion P3 and N2 data was increased from that of the NC group. Post-exercise the C group had a decrease in amplitude in both the P3 and N2. However, the results of the ERP analysis post-exercise revealed results that resembled the sample data used in both the P3 and N2. On the other hand, the results from the NC group, matched that of previous literature. There was an increase in P3 and N2 amplitude following exercise, with a prominent increase in the P3. One possible reason for this may be because different images were presented in the second block, so images were in a sense 'still novel' as active memory representations had not yet been made for the stimuli shown.

While the increase in P3 witnessed in the NC group is indicative of enhanced decision-making capabilities during target stimulus presentation, the opposing decrease in amplitude seen in our C group may be representative of a 'normalization' to levels similar to that of our NC group pre-exercise. Perhaps pre-exercise, our concussed participants processed information inefficiently and post-exercise they were more efficient. However, it had been hypothesized that post-exercise amplitudes would resemble that of the NC group pre-exercise. Although the data did not increase as expected with the NC group, our data did match that of the post-exercise

sample data implying in part, that our concussed group was more efficient at processing information related to task demands post-exercise.

Finally, it is important to note that there were minor differences in attentional patterns in each of the concussion participants. This may be due in part to their differences in concussion history. Each concussion seems to inflict unique damage that results in a variety of changes structurally and functionally. Studies in the future should focus on singular cases of concussion and their unique histories.

7.3.3 Theta, Alpha, Beta Power

Compared to data from Adams, the NC group followed the trends that were expected among controls pre-exercise (Adams et al., 2020). Participant 001 and 006 showed similar trends both frontally and parietally, however, participant 006 had much higher power in Pz compared to the controls. This data assures us that the pre-exercise data was similar to sample data and inferences can further be made post-exercise. Overall, there was a decrease in synchronization following exercise in all groups. The NC group, in disagreement with previous literature depicting an increase in theta, alpha, and beta frequencies, exhibited decreases in synchronization to target and non-target stimuli within these frequencies.

Dissimilar to the NC group, participant 001 increased in synchrony following exercise in the Fz electrode and desynchrony in all frequencies in the Pz electrode. Participant 006, like the NC group, showed decreases in synchrony in the Pz electrode site, but showed frequency increases frontally. Because each of the frequency bands are related to a different stream of processing, the differences in concussion may result in issues in a variety of brain regions and processes. The alpha frequency has been related to aspects of cognitive efficiency and decreases when attentional demands of a task increase (Guay et al., 2018; Hermann & Knight, 2018). Beta is

linked to the neural ensembles engage in a specific task (Barlow et al., 2018; Guay et al., 2018) and increase frontally when the difficulty of the task is increased (Kaufman et al., 2017).

Lastly, theta oscillations are associated with aspects of proactive control when the brain is preparing itself for goal directed behaviour (Guay at al., 2018; Hermann & Knight, 2018). With regards to the NC group, a decrease in frequency could indicated less of an attentional demand on the executive drive for the task at hand less effort is needed to achieve the same behavioural results following exercise (Barlow et al., 2018; Guay et al., Hermann & Knight, 2018). Literature surrounding ERSPs and concussion are commonly associated with a decrease in alpha and beta frequency (Guay et al., 2018). Our results show the opposite. Exercise potentiated the difference between target and non-target stimuli and the power was increased in the concussed group frontally which may indicate compensation during stimulus presentation. Coupled with the absence of behavioural performance changes, the abnormal alpha and theta band frequency following concussion provides additional support for the notion that EEG measure can reveal changes in brain activity that would otherwise go undetected based on behavioural performance measures (Guay et al., 2018). Further, more detailed studies on brain oscillations should be employed to better understand the changes following concussion.

7.3.4 Exercise

Significant amounts of research have been done on the effects of exercise and attentional correlates. Exercise has the ability to modulate cortical excitability, neuroplasticity, and cortical activation (Alves et al., 2014, Singh et al., 2014). Specifically with regards to neuroplasticity, exercise has been shown to decrease the amount of intracortical inhibition present in order to upregulate the mechanisms associated with plasticity (Bullock & Giesbrecht, 2014). The increase in P3 amplitude in the NC group post-exercise could be representative of these phenomena,

whereas the decrease in P3 present in the C group following exercise could indicate an inability to filter irrelevant incoming sensory information. Contrarily, the decrease seen in P3 and N2 amplitudes in the C group could constitute some kind of efficiency gain similar to that of the control group, including mechanisms in the thalamus responsible for connecting various pathways. Lastly, exercise helps to upregulate the excitability in the PFC promoting an increase in the top-down regulation of tasks (Popvich & Staines, 2015), increasing the efficiency of neural processing streams present in attention.

Finally, comparing our concussion data to similar studies done on the elderly provides insight into similar brain pattern changes, as well as changes following exercise. Pedroso and colleagues (2017) performed an EEG study on elderly participants following exercise. The researchers stated in their findings that exercise, especially aerobic or resistance training in old age, has marked beneficial effects on the P3 and N2. Literature on older adults states that there is a decrease in cognitive reserve is seen later in life (Gironell et al., 2015; McAllister & McCrae, 2017). Similarly, those who report concussion earlier in life show significant decline much earlier in life (Piirtola & Era, 2006). If older adults have improvements in their attentional correlates following a long-term exercise regime, it is plausible to suggest that those with concussion could benefit exercise throughout life. Long-term exercise could increase the amount of plasticity present, though brain derived neurotrophic factors, increasing the number of and strength of neural connections to create a larger more robust cognitive reserve. A larger cognitive reserve may aid in the slowing of accelerated aging and conserve cognitive efficiency, capability, and quality into older age.

8.0 Limitations

With any study in concussion, one of the hardest factors to control is subconcussive blows, or non-clinically diagnosed concussions. Although participants who formed the non-concussed group reported not participating in contact sports growing up, this does not mean that they are completely free from subconcussive damage - other factors may have led to damage that would go unseen otherwise. With regards to the concussion group, it is common for previous athletes to under report or distort their concussion history, so the extent of damage is likely misrepresented. As well, both concussion participants were of more extensive fitness backgrounds which may have resulted in skewing of the P3 and N2 data which are sensitive to changes in higher fit individuals. Another limitation present in our study was the means of determining overall fitness level and 70% of HR max. The IPAQ itself, although valid in larger study groups, has minimal validity across smaller groups and the results of the survey tend to be exaggerated, increasing the overall fitness level of the participants above what likely is their actual fitness level. With regards to determining exercise intensity, it would have been ideal to determine 70% HR max from a VO_2 max test rather than participants' age predicted max HR. Because of the inaccuracy of the HR max formula, a VO_2 test would have better predicted target HRs for the exercise condition.

Lastly, the largest limitation of this study was the lack of participants due to COVID-19. Because of circumstances out of our control, we were unable to recruit and test the number of participants needed to determine statistical significance among groups and across time points. Due to this situation, a case study approach was taken for our concussion group and connections were drawn. With a larger number of participants in both the concussed and non-concussed group, statistical analyses could have been preformed to determine actual significance between

factors. However, the trends observed in this study outline a framework for future research directions.

9.0 Conclusion and Future Directions

The prominent finding from this study is that moderate intensity exercise performed prior to an attentional task changes attentional correlates in those who have sustained a concussion differently than those who have not. This is an important finding for long-term concussion rehabilitation applications as it suggests that exercise could be used in conjunction with other methods of slowing cognitive decline in order to extend optimal cognitive functioning. Our results suggest that exercise may improve neural correlates on attentional tasks following exercise in those with concussion and may promote the return of these neural correlates back to a baseline level post-concussion. Other methods of exercise should be examined in order to make recommendations to those who are unable to participate in moderate intensity exercise on a regular basis.

In the future, research should aim to determine the exercise that is best suited to subserve improved cognition throughout life following concussion. Both amount and intensity should be examined to determine the best prescription. As well, exercise throughout life should be explored. Does exercise in older aged populations who have sustained concussions earlier in life aid in slowing the accelerated cognitive aging process? And is there a way to enhance cognitive reserve early in life to prolong the ability to perform tasks without the risk of behavioural changes?

Finally, future research should aim to determine how the known pathophysiology of concussion and the normal effect of aging on the brain could exacerbate each other. Currently, there is limited research on the pathophysiological effects of concussion and even less is available on the long-term structural effects of concussion. Those who have previously sustained

concussions should be studied both in groups (divided by number and length of symptomology), as well as on a case-by-case basis.

Research has come a long way even in the last 10 years, however there is still much to learn regarding the changes seen in the brain following concussion and even more to learn regarding the effects a concussion has on the human lifespan, and quality of cognition later into life.

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