EXPLORING THE NEUROPHYSIOLOGICAL EFFECT OF AEROBIC EXERCISE IN CONCUSSION: AN EEG FESABILITY STUDY

by

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The following individuals certify that they have read, and recommend to the Faculty of Graduate and Postdoctoral Studies for acceptance, a thesis entitled:

Exploring the neurophysiological effect of aerobic exercise in concussion: An EEG feasibility study

submitted by Patrick O’ Flaherty in partial fulfillment of the requirements for the degree of Master of Science in Rehabilitation Sciences

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Abstract

Concussion is a complex and dynamic injury that involves alterations in brain function. This can present clinically as post-concussive symptoms and exercise intolerance. However, functional brain changes can extend beyond the point of clinical recovery. This can lead to increased brain vulnerability when returning to play as complete physiological recovery has not yet been achieved. Neuroimaging techniques such as Electroencephalography (EEG) can quantify functional brain changes that are present after sustaining a concussion. Despite advances in neuroimaging techniques, there is a paucity of research evaluating the effect exercise has on brain function following a concussion. The aim of this feasibility study was to evaluate functional brain changes as measured by EEG spectral power in a group of concussed participants in comparison to healthy controls before and after performing a clinical exertion test entitled the Buffalo Concussion Bike Test (BCBT). A secondary aim was to evaluate behavioral differences between the two groups.

The study consisted of five concussed and five control participants. Results revealed increased power in the 1-14 frequency range (delta, theta, alpha and low beta) in frontal brain regions of the concussed group in comparison to controls before and after performing the BCBT. EEG data collection was on average 90 to 120 minutes in duration and data quality was high for the majority of participants (83%). Three concussed participants failed the BCBT due to exceeding heart rate criteria, one failed due to symptom increase and one passed the test. Results indicate the feasibility of EEG spectral power as a measure of functional brain changes post-concussion, however, the BCBT may not be a suitable concussion exertion protocol for a non-athlete population. For behavioral measures, we found clear group differences when comparing results between concussed and control groups.
Lay Summary

Electroencephalography (EEG) is a neuroimaging technique that measures brain function. After sustaining a concussion there are alterations in brain function that can present as post-concussion symptoms and an inability to exercise. However, symptom resolution can occur in the absence of brain recovery which potentially predisposes the brain to further injury when returning to sports or activities. The aim of this study was to evaluate if it was feasible to measure brain function using EEG in a group of concussed participants in comparison to healthy controls before and after performing a clinical exercise test called the Buffalo Concussion Bike Test (BCBT). A secondary aim was to assess if there were behavioral differences between the concussed and control group. Results indicate it was feasible to measure brain changes using EEG before and after performing the BCBT and that clear behavioral differences were present between the two groups.
Preface

This thesis contains the work of a research study conducted by Patrick O’ Flaherty under the supervision of Dr. Naznin Virji-Babul with guidance from Dr. Noah Silverberg and Dr. William Panenka. The study procedures were performed according to the guidelines of the Clinical Research Ethics Board at the University of British Columbia. The Clinical Research Ethics Board Certificate Number is H19-01156. The study design and protocol were developed by Patrick O’ Flaherty and Dr. Naznin Virji Babul and with the assistance of Dr. Noah Silverberg and Dr. William Panenka. Data Collection and analysis was completed by Patrick O’ Flaherty.
Table of Contents

Abstract.................................................................................................................................................. iii
Lay Summary ........................................................................................................................................ iv
Preface.................................................................................................................................................. v
Table of Contents ................................................................................................................................ vi
List of Tables ....................................................................................................................................... x
List of Figures ..................................................................................................................................... xi
List of Symbols .................................................................................................................................. xii
List of Abbreviations ........................................................................................................................ xiii
Acknowledgements ........................................................................................................................... xvi
Dedication ........................................................................................................................................... xvii

Chapter 1: Introduction ..................................................................................................................... 1
  1.1 Purpose........................................................................................................................................ 1
  1.2 Definition of a Concussion ........................................................................................................... 2
  1.3 Symptom Presentation ................................................................................................................. 3
  1.4 Epidemiology .............................................................................................................................. 4

Chapter 2: Background ....................................................................................................................... 7
  2.1 Introduction ................................................................................................................................ 7
    2.1.1 Pathophysiology .................................................................................................................. 7
    2.1.2 Autonomic Dysfunction ...................................................................................................... 8
  2.2 Management of Concussion ........................................................................................................ 10
    2.2.1 Return to Play ...................................................................................................................... 11
    2.2.2 Neurocognitive Assessment .............................................................................................. 12
2.2.3 Exercise Assessment ........................................................................................................ 13

Chapter 3: Electroencephalography ...................................................................................... 15

3.1 Introduction ...................................................................................................................... 15
3.2 EEG Spectral Analysis ..................................................................................................... 16
3.3 EEG Source Analysis ...................................................................................................... 19
3.4 EEG Measures in Concussion ....................................................................................... 21
3.5 Extraneous Factors Influencing EEG Measures .............................................................. 25
3.6 Aims and Hypotheses ..................................................................................................... 26

Chapter 4: Methodology ........................................................................................................ 28

4.1 Study Overview ................................................................................................................... 28
  4.1.1 Participants .................................................................................................................. 28
4.2 Study Procedure ................................................................................................................ 29
  4.2.1 Self-Report Measures ................................................................................................. 29
  4.2.2 Symptom Scale ......................................................................................................... 30
  4.2.3 Modified Balance Error Scoring System .................................................................. 30
  4.2.4 Vestibular and Ocular Motor Assessment ................................................................. 31
4.3 Exertion Protocol .............................................................................................................. 32
4.4 EEG Data Collection ....................................................................................................... 34
  4.4.1 EEG Data Analysis .................................................................................................... 35
4.5 Statistical Analysis .......................................................................................................... 36

Chapter 5: Results .................................................................................................................. 38

5.1 Participant Characteristics ................................................................................................. 38
5.2 Behavioral Measures ......................................................................................................... 39
5.3 Post-Concussion Symptom Scale ................................................................. 40
5.4 Balance and Vestibular/Ocular Motor Measures .......................................... 44
5.5 Exertion Protocol ......................................................................................... 44
5.6 EEG Data ...................................................................................................... 46
  5.6.1 Sensor-Space Results .............................................................................. 46
  5.6.2 Source-Space Results ............................................................................. 51
    5.6.2.1 Overall average power between groups pre and post-exertion ....... 51
    5.6.2.2 Overall average power within groups pre and post-exertion ......... 51
    5.6.2.3 Frequency bands .............................................................................. 51
    5.6.2.4 Brain regions ................................................................................... 52

Chapter 6: Discussion .......................................................................................... 55
  6.1 EEG Feasibility ............................................................................................ 55
  6.2 Behavioral Measures ................................................................................... 60
  6.3 Strengths, Limitations and Future Directions ............................................ 62

Chapter 7: Conclusion ......................................................................................... 65

References ........................................................................................................... 66

Appendices .......................................................................................................... 82
  Appendix A: Advertisement to Recruit Participants ....................................... 82
  Appendix B: Consent Form ............................................................................... 83
  Appendix C: Demographic Information and Past Medical History ............... 90
  Appendix D: PAR-Q+ ...................................................................................... 92
  Appendix E: Sleep Condition Indicator ........................................................... 96
  Appendix F: Fear Avoidance after Traumatic Brain Injury Questionnaire .... 97
Appendix G: Symptom Scale........................................................................................................98
Appendix H: Vestibular/Ocular Motor Screening ................................................................. 99
Appendix I: BORG Rating of Perceived Exertion ................................................................. 100
Appendix J: Buffalo Concussion Bike Test ........................................................................ 102
List of Tables

Table 5.1.1: Participant characteristics. .......................................................... 39
Table 5.2.1: SCI scores for all participants. ...................................................... 40
Table 5.2.2: FAB-TBI scores for all participants. ............................................. 40
Table 5.4.1: VOMS and mBESS scores for concussed group. ....................... 44
Table 5.5.1: BCBT results for the control group. ............................................ 45
Table 5.5.2: BCBT results for the concussed group. ........................................ 45
Table 5.5.3: Heart rate measures for the exertion protocol............................. 45
List of Figures

Figure 3.2.1: Graphical representation of an EEG power spectrum........................................... 17
Figure 3.2.2: Decomposition of EEG signals into different frequency bands................................. 19
Figure 3.3.1: Illustration of a virtual source montage........................................................................ 21
Figure 4.4.1: Locations of electrode placement on the scalp for an EEG ....................................... 35
Figure 5.3.1: Concussed and control participants total symptom scores........................................... 42
Figure 5.3.2: Concussed and control participants total symptom severity scores............................. 42
Figure 5.3.3: Concussed and control groups average total symptom scores................................... 43
Figure 5.3.4: Concussed and control groups average total symptom severity scores....................... 43
Figure 5.6.1: Average and individual PSD for control participants pre and post-exertion................. 47
Figure 5.6.2: Average and individual PSD for concussed participants pre and post-exertion............. 48
Figure 5.6.3: Control and concussed groups average PSD.............................................................. 49
Figure 5.6.4: Control and concussed groups scalp topographies.................................................... 50
List of Symbols

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$r$</td>
<td>Correlation Coefficient</td>
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<tr>
<td>$°$</td>
<td>Degrees</td>
</tr>
<tr>
<td>$=$</td>
<td>Equals</td>
</tr>
<tr>
<td>$\Delta$</td>
<td>Glass’s $d$</td>
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<tr>
<td>$&gt;$</td>
<td>Greater than</td>
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<tr>
<td>$g$</td>
<td>Hedge’s $g$</td>
</tr>
<tr>
<td>$k\Omega$</td>
<td>Kilo-ohm</td>
</tr>
<tr>
<td>$&lt;$</td>
<td>Less than</td>
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<td>$\mu V$</td>
<td>Microvolts</td>
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<td>*</td>
<td>Multiply</td>
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<td>/</td>
<td>Per</td>
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<tr>
<td>$%$</td>
<td>Percent</td>
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<tr>
<td>$\pm$</td>
<td>Plus-minus</td>
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<tr>
<td>$^2$</td>
<td>Squared</td>
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<tr>
<td>$\sqrt{}$</td>
<td>Square root</td>
</tr>
<tr>
<td>$v$</td>
<td>Version</td>
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### List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ADHD</td>
<td>Attention Deficit-Hyperactivity Disorder</td>
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<td>AE</td>
<td>Athlete-Exposure</td>
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<tr>
<td>ANS</td>
<td>Autonomic Nervous System</td>
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<tr>
<td>ATP</td>
<td>Adenosine Triphosphate</td>
</tr>
<tr>
<td>BCBT</td>
<td>Buffalo Concussion Bike Test</td>
</tr>
<tr>
<td>BCTT</td>
<td>Buffalo Concussion Treadmill Test</td>
</tr>
<tr>
<td>BPM</td>
<td>Beats per Minute</td>
</tr>
<tr>
<td>CA</td>
<td>Cerebral Autoregulation</td>
</tr>
<tr>
<td>CBF</td>
<td>Cerebral Blood Flow</td>
</tr>
<tr>
<td>CISG</td>
<td>Concussion in Sport Group</td>
</tr>
<tr>
<td>CO$_2$</td>
<td>Carbon Dioxide</td>
</tr>
<tr>
<td>CNT</td>
<td>Computerized Neurocognitive Test</td>
</tr>
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<td>CT</td>
<td>Computed Tomography</td>
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<td>DFT</td>
<td>Discrete Fourier Transform</td>
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<tr>
<td>DLPC</td>
<td>Dorsolateral Prefrontal Cortex</td>
</tr>
<tr>
<td>DMN</td>
<td>Default Mode Network</td>
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<tr>
<td>DTI</td>
<td>Diffusion Tensor Imaging</td>
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<tr>
<td>EEG</td>
<td>Electroencephalography</td>
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<tr>
<td>EPSP</td>
<td>Excitatory Postsynaptic Potential</td>
</tr>
<tr>
<td>ES</td>
<td>Effect Size</td>
</tr>
<tr>
<td>FAB-TBI</td>
<td>Fear Avoidance Behavior after Traumatic Brain Injury</td>
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<tr>
<td>FFT</td>
<td>Fast Fourier Transform</td>
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<tr>
<td>Abbreviation</td>
<td>Definition</td>
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<tr>
<td>HR</td>
<td>Heart Rate</td>
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<tr>
<td>HRt</td>
<td>Heart Rate threshold</td>
</tr>
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<td>HRV</td>
<td>Heart Rate Variability</td>
</tr>
<tr>
<td>Hz</td>
<td>Hertz</td>
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<tr>
<td>ICA</td>
<td>Independent Component Analysis</td>
</tr>
<tr>
<td>ImPact</td>
<td>Immediate Post Concussion Assessment and Cognitive Test</td>
</tr>
<tr>
<td>IPSP</td>
<td>Inhibitory Postsynaptic Potential</td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile Range</td>
</tr>
<tr>
<td>mBESS</td>
<td>Modified Balance Error Scoring System</td>
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<tr>
<td>Mdн</td>
<td>Median</td>
</tr>
<tr>
<td>mL</td>
<td>Milliliter</td>
</tr>
<tr>
<td>mmHg</td>
<td>Millimeter of Mercury</td>
</tr>
<tr>
<td>MOI</td>
<td>Mechanism of Injury</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>mTBI</td>
<td>Mild Traumatic Brain Injury</td>
</tr>
<tr>
<td>NCAA</td>
<td>National Collegiate Athletic Association</td>
</tr>
<tr>
<td>NPC</td>
<td>Near Point of Convergence</td>
</tr>
<tr>
<td>PAR-Q+</td>
<td>Physical Activity Readiness Questionnaire</td>
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<tr>
<td>PCSS</td>
<td>Post-Concussion Symptom Scale</td>
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<tr>
<td>PNS</td>
<td>Parasympathetic Nervous System</td>
</tr>
<tr>
<td>PPCS</td>
<td>Persistent Post-Concussion Symptoms</td>
</tr>
<tr>
<td>PSD</td>
<td>Power Spectral Density</td>
</tr>
<tr>
<td>REM</td>
<td>Rapid Eye Movement</td>
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<tr>
<td>Acronym</td>
<td>Full Form</td>
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<tr>
<td>ROI</td>
<td>Regions of Interest</td>
</tr>
<tr>
<td>RPM</td>
<td>Revolutions per Minute</td>
</tr>
<tr>
<td>rs-EEG</td>
<td>Resting-state Electroencephalography</td>
</tr>
<tr>
<td>RTP</td>
<td>Return to Play</td>
</tr>
<tr>
<td>SCI</td>
<td>Sleep Condition Indicator</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SNS</td>
<td>Sympathetic Nervous System</td>
</tr>
<tr>
<td>SPECT</td>
<td>Single-Photon Emission Computed Tomography</td>
</tr>
<tr>
<td>SRC</td>
<td>Sports-Related Concussion</td>
</tr>
<tr>
<td>SSRI</td>
<td>Selective Serotonin Reuptake Inhibitor</td>
</tr>
<tr>
<td>TBI</td>
<td>Traumatic Brain Injury</td>
</tr>
<tr>
<td>VOMS</td>
<td>Vestibular/Ocular Motor Screening</td>
</tr>
<tr>
<td>VOR</td>
<td>Vestibulo-Ocular Reflex</td>
</tr>
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</table>
Acknowledgements

I would like to express sincere gratitude to my supervisor, Dr. Naznin Virji-Babul for allowing me the opportunity to pursue my degree and providing me with support and guidance throughout my studies. It has been a fantastic learning experience. I would also like to thank Dr. Noah Silverberg and Dr. William Panenka for their advice and expertise.

I offer a special thanks to past and present fellow lab mates, Rebecca Kenny, Ella Weik, Leyla Brucar and Naama Rotem-Kohavi, whose advice and knowledge was truly appreciated. Thank you all.
Dedication

To my parents and sister for providing me with endless support, encouragement and love.

Thank you so much.

To Mam, A Stór Mo Chroí.
Chapter 1: Introduction

1.1 Purpose

The purpose of this thesis is to evaluate changes in brain function using resting-state electroencephalography (rs-EEG) in a group of concussed participants in comparison to healthy controls before and after performing a graded exertion test entitled the Buffalo Concussion Bike Test (BCBT).

Concussion and mild traumatic brain injury (mTBI) have gained increased attention and exposure in medical, athletic and research communities in recent years. Focus has also grown in the public domain with increased media coverage and legislation passed (1,2). There has been a greater incidence rate of concussion in the last 10 years which has prompted an influx of research studies in the scientific literature (3). However, research has yet to yield an objective diagnosis for concussion, with a strong reliance on subjectivity relating to the mechanism of injury (MOI) and ensuing sequela of post-concussive symptoms (4,5). Symptom reporting is also used as an indicator of concussion recovery and in the management of return to play (RTP) (6). However, the time frame for physiological recovery can outlast clinical recovery, which may predispose athletes to further injury (1,4,5,7).

To improve our current understanding of concussion recovery and subsequent management, there is a need for more quantitative and objective measures that can better inform both patient and clinician. In particular, questions remain unanswered with concussion as it pertains to exercise such as: What effect does exercise have on brain function in concussion? Is there a difference in brain function in concussed participants in comparison to healthy controls after performing exercise? The current study will aim to provide answers to these questions to help improve our understanding of concussion. Before discussing these topics, it is important to
first define concussion, discuss the ensuing symptom presentation and provide a contextual background about the epidemiology of concussion.

1.2 Definition of a Concussion

The terms concussion and mTBI are often used interchangeably in both clinical and research settings. The latter is associated with the non-athlete population and is defined by a Glasgow Coma Scale score of 13-15 with limited post-traumatic amnesia and the absence of abnormal neuroimaging, this permits differentiation from moderate to severe forms of TBI (8,9). Although the MOI may differ between sports-related concussion (SRC) and mTBI, the underlying pathophysiology is consistent (10,11). To provide a more robust definition amongst medical professionals and researchers the development of consensus statements on concussion were established. The most recent conference by the Concussion in Sport Group (CISG) was held in Berlin in 2016, where a definition of SRC was defined by the following characteristics:

(1) SRC may be caused either by a direct blow to the head, neck, face or elsewhere in the body with an impulsive force transmitted to the head.

(2) SRC typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously. However, in some cases, signs and symptoms evolve over several minutes to hours.

(3) SRC may result in neuropathological changes, but the acute clinical signs and symptoms largely reflect a functional disturbance rather than a structural injury and, as such, no abnormality is seen on standard structural neuroimaging studies.
(4) SRC results in a range of clinical signs and symptoms that may or may not involve loss of consciousness. The resolution of the clinical and cognitive features typically follows a sequential course. However, in some cases, symptoms may be prolonged (4).

A similar definition is provided by the American Medical Society for Sports Medicine by defining concussion as a traumatically induced transient disturbance of brain function involving a complex pathophysiological process (1). This alteration in brain function may or may not present with loss of consciousness along with post-traumatic amnesia (12).

1.3 Symptom Presentation

After sustaining a concussion symptom resolution normally occurs within 7 to 10 days, however, in approximately 30% of the population symptoms can persist and are subsequently defined as persistent post-concussion symptoms (PPCS) (13,14). Symptom presentation is heterogeneous and can affect different clinical domains. Some of the signs and symptoms typically encountered after sustaining a concussion can include physical (headache, fatigue, dizziness, gait disturbance), physiological (exercise intolerance), ocular (sensitivity to light, blurred vision, eye strain), cognitive (executive functioning, memory, concentration problems), affective (depression, anxiety, emotional lability) and sleep disturbance (hypersomnia, insomnia) (1,15).

Currently there is no objective gold standard criteria for concussion diagnosis. A diagnosis is usually performed from a multimodal approach through clinical evaluation involving the MOI and administration of a battery of tests including subjective symptom reporting, neurocognitive testing and physical assessment such as balance and exertion testing (16).
Symptoms are commonly reported using a standardized scale such as the Post-Concussion Symptom Scale (PCSS), which consists of a 22-item inventory scale ranging from 0 (none) to 6 (severe) and details symptom presentation in the aforementioned clinical domains. However, a limitation of this measure is a focus on the total number of symptoms and not on symptom specificity. For example, after sustaining a concussion, increased levels of dizziness alone is associated with a protraction in recovery time by six-fold (16). Other factors such as genetics, age, sex, premorbid illness and a prior history of concussion can elongate recovery also, with children and adolescents, specifically females, experiencing the highest rate of symptoms and protracted recovery (17,18).

1.4 Epidemiology

The prevalence rates of SRC have been estimated at 1.6 to 3.8 million annually in the United States, however, this number may be higher than estimated due to unreported and undiagnosed cases (19,20). Increased awareness, knowledge translation and new legislation has facilitated recognition of concussion and contributed to a lower threshold of diagnosis (2). According to the Center for Disease Control and Prevention, an estimated 75% of 2.5 million emergency department visits are due to mTBI (21). Willer and colleagues (22) reported head injury rates of 3.98 per 100 for children aged 6-16 in Canadian schools in Ontario. Young children presented with more head injuries than older children, with the predominant MOI sustained from falls. Findings from an evaluation of the Canadian National Population Health Survey found a rate of concussion of 110 per 100,000 (23). An increased rate of concussion was reported for younger individuals with 200/100,000 for 0-14 years, 160/100,00 for 15-34 years and 50/100,000 for 35 years or older. SRC was the most common MOI with an incidence rate of
over 54% and over 85% of concussions in the 15-34-year-old group were sustained from playing sports. Sex-related incidences were higher in males (140/100,000) compared to females (80/100,00). However, in a review by Koerte and colleagues (12), studies indicate that females have a more prolonged recovery trajectory and worse outcomes compared to males. This may be caused by differences such as decreased neck girth and strength as well as physiological and hormonal variations (4).

Differences in incidence rates vary between sports with men’s American football consistently rated highest (36.1%), followed by men’s ice hockey (13.4%) and women’s soccer (8.1%) (3, 24). Marshall and colleagues (25) reported increased incidence rates for American football compared to six other U.S high school and collegiate sports. Similar findings were reported in a systematic review where 19 of the 33 prospective studies consisted of concussions sustained from American football, with an 87.3% incidence rate of adolescent and young male athletes (16). In high school, concussion accounts for 9-13% of all reported injuries with the top 3 sports being rugby, ice hockey and American football (4.18, 1.20 and 0.53 athlete-exposure (AE) per 1000) (26, 27). AE is an athlete’s participation method equating to 1 athlete participating in 1 practice or game.

Men’s wrestling (10.92/1000 AE) and women’s ice hockey (7.50/1000 AE) were reported to surpass the incidence rate of collegiate football (6.71/1000 AE) in a descriptive epidemiological study conducted on National Collegiate Athletic Association (NCAA) sports from 2009-2010 to 2013-2014 (28). In this study approximately 53% of all concussions sustained by NCAA athletes occurred during competition and concussion alone represented 6% of all collegiate athletic injuries (28, 29). In another NCAA study (30), it was reported that athletes who sustained a concussion were three times more likely to sustain a second concussion in the same
season compared to athletes who did not have a concussion history. Furthermore, 91.7% of the repeated concussions occurred within 10 days of the first injury. However, a recent update conducted by the NCAA-Department of Defense Concussion Assessment, Research and Education (CARE) Consortium from 2014 to 2017 reported a 41% reduction in the rate of same-season repeat concussions (31). Findings also indicated a significant increase of 10 additional days before athletes returned to play compared to the previous study. This signifies improvements in the clinical management of concussion over the past 15 years in respect to the risk of repetitive injury following the critical period of cerebral vulnerability. It is therefore of utmost importance to understand the physiological impairments at play during this critical period and the management strategies that are currently employed for RTP as will be discussed in the following chapter.
Chapter 2: Background

2.1 Introduction

Before reviewing the literature on concussion and EEG outcomes, it is necessary to first discuss the physiological impairments involved following a concussion to better understand why dysfunction in exercise tolerance can occur. Injury pathophysiology will be discussed followed by an overview of the physiological impairments at play post-concussion. This will be followed by current management strategies for RTP including exertion testing involving the BCBT. Lastly, in chapter two, an overview of EEG will be provided followed by a review of the literature as it relates to concussed populations thus providing a framework for the current study.

2.1.1 Pathophysiology

Concussion represents a functional disturbance of the brain that involves microscopic neural damage, therefore conventional neuroimaging techniques such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are unable to clearly delineate structural neural anomalies (10,32,33). However, novel imaging techniques such as Diffusion Tensor Imaging (DTI) have found axonal damage in brain regions such as the corpus callosum which is a key region for inter-hemispheric integration of sensory, motor and cognitive information (34). Following an injury to the brain, there are alterations in the cellular environment with Giza and Hovda (33) coining the phrase ‘the neurometabolic cascade of concussion’. Functional alterations to cellular or physiological function can include ionic shifts, neurometabolic changes such as an increase in glucose metabolism (hyperglycolysis) and impaired function in neurotransmission. The neurometabolic cascade initiates an ionic flux and depolarization with the release of the excitatory neurotransmitter glutamate (35). Ionic
fluctuations occur when potassium exits and calcium enters the cells, resulting in changes in cellular physiology such as vasoconstriction, alterations in cerebral blood flow (CBF) and an increase in cerebral glucose metabolism. Consequently, the sodium-potassium pump attempts to maintain homeostatic cell membrane permeability which requires increased amounts of adenosine triphosphate (ATP) and results in a metabolic energy crisis (33,36).

After the initial period of hyperglycolysis, impairments in metabolism can last up to 10 days, corresponding to the typical timeline of symptom resolution (4,5,10). During this vulnerable period, there is a decrease in the brains ability to adequately respond to a second concussive blow and an increased susceptibility to re-injury (10,33). Much of the mitochondrial dysfunction following a concussion is related to prolonged cellular exposure to high levels of calcium (36). This disruption in mitochondrial activity inhibits the production of ATP and can lead to cellular necrosis and death via apoptosis (37). Animal models have predominately provided information regarding the neurophysiological response to concussion and therefore the severity of the injury can be greater when extrapolated to a human population. Ellis and colleagues (14) have suggested that concussion pathophysiology may be caused by impairments in specific neurological sub-systems such as the cervicogenic and vestibulo-ocular systems or at a more global cellular level in the form of autonomic dysfunction which will be discussed next.

2.1.2 Autonomic Dysfunction

The Autonomic Nervous System (ANS) is composed of two complementary systems called the Sympathetic Nervous System (SNS) or the "fight or flight system" and the Parasympathetic Nervous System (PNS) or the "rest and digest system" (38). The ANS is responsible for many homeostatic functions including the regulation of cardiac and smooth
muscle contractility to brain tissue via the baroreflex (39). The ability to maintain constant perfusion in cerebral tissue in response to fluctuations in perfusion pressure, such as when exercising, is known as dynamic cerebral autoregulation (CA). A review of the literature relating to autonomic dysfunction or dysautonomia in mTBI concluded that impairments in CA regulation are seen in both the acute and subacute stage post-injury (40). Dysautonomia increases sympathetic neural activation which contributes to neuroinflammation, oxidative stress and CBF impairments (40). This can manifest clinically with symptom presentation such as headaches, anxiety, cognitive impairments and exercise intolerance (41). Uncoupling of the ANS is measured through various techniques such as heart rate variability (HRV), pupillary dynamics, eye pressure, arterial pulse wave and graded exercise testing (40,41).

Clausen and colleagues (42) evaluated dysautonomia by measuring CBF velocity with transcranial doppler ultrasonography during a graded exercises test on a treadmill in 9 female athletes experiencing PPCS. Findings indicated statistically significant decreased arterial carbon dioxide (CO₂) sensitivity in the concussed group (1.35 ± 2.11 L/min/mmHg CO₂) in comparison to the control group (2.88 ± 0.60 L/min/mmHg CO₂). This altered CO₂ sensitivity blunted the ventilation response during exercise, which in turn increased arterial CO₂ and CBF velocity in the concussed group correlating with increased symptom presentation of headache and dizziness and thus limited exercise tolerance. These findings indicate impaired CBF velocity may be due to decreased CO₂ sensitivity and alterations in CA after a concussion. CBF is an important indicator of neuronal function, with impairments potentially leading to alterations in functional integrity in the brain (40).

HRV is also used as an indirect measure of ANS function and reflects the total variation of consecutive HRs or more specifically the standard deviation of consecutive
heartbeats of the R-R intervals (39,41). Increased HRV is associated with adaptation to physiological requirements and is considered a putative marker for effective ANS modulation (41). Gall et al (43) found HRV to be decreased 5 days post-concussion when performing low-to-moderate intensity exercise on a cycle ergometer. In contrast, no difference in HRV was found at rest in the concussed group compared to controls. Reduced HRV has been associated with exercise intolerance and decreased pre-frontal cortical activity (40). This may have implications for the presentation of exercise intolerance and cognitive complaints after sustaining a concussion.

2.2 Management of Concussion

An initial period of 24 to 48 hours of physical and cognitive rest is advocated post-concussion (44). During this vulnerable period, the brain is undergoing an "energy crisis" and prematurely returning to activities can have deleterious effects on recovery such as reducing neuroplasticity and predisposing the athlete to a risk of re-injury or the more fatal second impact syndrome (6,33,44). However, after this initial period, strict rest or “cocoon therapy” is associated with slower recovery rates and increased levels of stress, anxiety, depression, irritability and physical deconditioning (1,45). Establishing an exact period of rest post-concussion remains elusive due to undefined prognostic factors and the heterogeneous nature of concussion. It is therefore recommended that a multifaceted management approach involving symptom monitoring, neurocognitive assessment, and physical and exertion testing be implemented (4,8,16,44).
2.2.1 Return to Play

Returning to activities or play after concussion involves a graduated approach to ensure an individual’s safety and to mitigate the risk of re-injury. Exercise is a form of physical activity usually performed recreationally that involves a plan, structure and repetition leading to the objective of maintaining or improving physical fitness (46). In contrast, sporting activities encompass a set of rules or goals to train and excel in specific athletic skills competitively. Examples include individual sports such as skiing or team sports such as football. For the latter, the CISG recommend a stepwise graduated RTP protocol which is guided by clinical evaluation and symptom reporting (6). The RTP protocol involves: 1) no physical/sporting activity, 2) light aerobic exercise, 3) sport-specific activities, 4) non-contact training drills, 5) full-contact practice and eventually RTP (4). Twenty-four hours is recommended between each stage, approximating one week before unrestricted RTP is allowed. Symptoms are reported at each stage of the protocol and progression is dictated by symptom resolution along with objective measurements of neurocognitive and balance function (4,6).

However, the protocol is currently not validated for progression sequence or time spent at each stage and is guided by individual subjective reporting to assess recovery (1). Although self-report symptom scales and checklists such as the PCSS are shown to have good validity, they are limited by the presentation of exercise-induced symptoms that are not due to concussion (8,47,48). In fact, in non-concussed populations, there can be a prevalence of symptom provocation that presents as concussive symptoms after completing moderate-intensity exercise (49). This has prompted recent consensus guidelines by the CISG to evaluate symptomology 15 minutes after exercising (4). However, there is limited evidence to support this time specification for symptom reporting (50). The psychometric properties of self-reported symptom scales are
further challenged by athletes inaccurately reporting symptoms in order to RTP and inter-day variability affective states rather than a direct relationship to the neurological insult of a concussion (20,51).

2.2.2 Neurocognitive Assessment

Impairments in cognitive function such as speed of information processing, visual and verbal memory and executive functioning are some of the common symptoms encountered post-concussion (16). Frontal lobe dysfunction relating to the dorsolateral prefrontal cortex (DLPC) and the default mode network (DMN) have been implicated in neuroimaging studies (52–54). Neurocognitive testing is considered the cornerstone of concussion diagnoses and management (16,55). Assessment of cognitive function is typically administered by the neuropsychologist and consists of a battery of tests such as questionnaires and computerized neurocognitive tests (CNTs) that assess different cognitive domains.

However, the test-retest reliability of CNTs in determining a diagnosis has been challenged, with a meta-analysis reporting both false-positive and false-negative results (56). The former has been estimated to occur in 40% to 80% of tests in a systematic review conducted on the most commonly administered CNT, the Immediate Post Concussion Assessment and Cognitive Test (ImPACT) (55). In another study, CNT results found one or more subtests below average in 48% of asymptomatic athletes (n=117) who were following RTP guidelines (57). However, these results had no relationship with successfully completing the RTP protocol. Confounding factors such as age, education, sleep habits, drug intake, motivation, language, practice effects and length of time between testing can play a significant role in test results (16,56). Due to the poor reliability of CNTs, inaccurate decisions may lead to either an
unnecessary protraction of recovery time or a premature RTP. This can have serious consequences for the physical and psychological wellbeing of the individual or of more concern, a risk of re-injury (1).

2.2.3 Exercise Assessment

Exercise tolerance is defined as the ability to complete exercise to one’s predicted age and ability without developing concussive symptoms or as the heart rate threshold (HRt) at symptom exacerbation (58–60). It has emerged as both a determinant for recovery and as an intervention in the management of concussion (1,6,44,61). As mentioned previously, factors such as ANS dysfunction and CBF impairment have been implicated in concussion for the presentation of exercise intolerance (39,42). However, specific neurological sub-systems such as the cervicogenic and vestibulo-ocular motor system may also present with exercise intolerance due to symptom presentation such as dizziness, headaches and pain (62).

The Buffalo Concussion Treadmill and Bike Tests (BCTT and BCBT) are graded exertion tests based on exercise tolerance (62,63). Symptoms, HR, and rating of perceived exertion (RPE) are monitored throughout the tests providing objective measurements of physiological function in response to exercise. Participants with ANS dysfunction will typically experience increased symptom presentation during the tests and be forced to stop prematurely. Physiological dysfunction would then be implied as a domain of concussive impairment. Studies exploring the use of the BCTT and BCBT have primarily focused on their prognostic utility for concussion recovery. Findings from such studies include an association of protracted recovery with a HRt of < 135 beats per minute (bpm) at symptom exacerbation (60). A lower HRt on initial assessment has also been associated with an increase in recovery time (60). Another study
evaluated the difference between resting HR and HRt using the BCTT and found that a value of ≤50 bpm is 73% sensitive and 78% specific for predicting a protracted recovery (64). In a retrospective study, Darling and colleagues (57) reported a safe and successful RTP for 117 concussed athletes aged between 13 to 19 years with the implementation of the CISG consensus statement guidelines and the BCTT. The BCTT has also been shown to be safe to administer within 1 week of injury, demonstrating no negative effects on concussion recovery (60).

Despite the clinical and prognostic utility of exercise tolerance, limitations such as fitness level, emotional status, attitude, motivation, time of day and sleep quality can confound results (64). Furthermore, the aforementioned studies predominately consisted of cohorts of adolescent athletes and thus results cannot be extrapolated to the general population. Although exercise testing can differentiate physiological impairment from cervicogenic or vestibular/ocular motor impairments, there is limited research identifying functional brain activity in response to exercise in a concussed cohort (17). Also, recovery was defined as being asymptomatic or returning to a “normal level of symptoms” in these studies which does not imply that impairments in brain function are not still present. One would expect there to be a more pronounced response in the concussed versus non-concussed brain after exercising especially in the acute stage as neurometabolic adaption has not yet been achieved. Also, if a concussion is representative of impairments relating to distinctive domains or systems, it could be hypothesized that exercise would induce a greater physiological demand on brain function in a cohort of exercise intolerant concussed participants who present with PPCS. The current study will aim to potentially identify these functional brain changes using EEG which will be discussed in the following chapter.
Chapter 3: Electroencephalography

3.1 Introduction

EEG has emerged as a valuable non-invasive tool to measure neurophysiological deficits stemming from a concussion (18,65,66). It was first developed in 1924 by German neuropsychiatrist Hans Berger. In a seminal paper, Berger reported the presence of brain oscillations recorded whilst the subject’s eyes were closed and in a relaxed state. He termed the oscillations alpha waves (67). EEG has subsequently been used to analyze brain processes in different physiological states such as sleep, under anesthetic and in the diagnoses of certain neural pathologies such as epilepsy (67,68). Measured using electrodes placed on the scalp, EEG is the graphical representation of the difference in voltage between two different cerebral locations plotted over time (69).

Neurons have high concentrations of potassium and chloride ions located inside the membrane, whilst sodium and calcium ions are located outside. Depolarization is said to occur when the membrane potential is propagated by an influx of positively charged ions, in contrast to hyperpolarization, which occurs with negative membrane potential influx (70). These action potentials initiate neurotransmitter activation along the nerve fiber triggering either an excitatory postsynaptic potential (EPSP) or an inhibitory postsynaptic potential (IPSP), which signifies the source of scalp-recorded EEG signals (70,71). EEG measures the local current flow of the EPSPs and IPSPs from pyramidal neurons in the cortex. The pyramidal neurons create electrical dipoles between the soma (body of neuron) and apical dendrites (branches of the neuron) with a process of ionic flux giving rise to the EEG recording (66,67). Recordable electrical activity can only be obtained from a large sample of active neurons measured within the cerebral cortex (71).
EEG is said to characterize large scale temporal and spatial disturbances (67,69). Fast
dynamic cortical activity such as sensorimotor and cognitive functions can be measured within
milliseconds with EEG due to its high temporal resolution (72). However, spatial resolution is
low due to the small number of spatial data samples, inherent volume conduction effect and
physiological or environmental artifacts (72). This inhibits the ability of EEG to measure deeper
cortical regions such as the cerebellum and brain stem (66). The major advantages of EEG in
comparison to other neuroimaging modalities include its high temporal resolution, non-invasive
application, portability and it is time and cost-efficient thus making it a viable
neurophysiological modality in the study of brain function following a concussion (65,68). An
important measurement in EEG is spectral power which will be discussed next.

3.2 EEG Spectral Analysis

Brain oscillations conform to a sinusoidal wave pattern and range in amplitude from 0.5
to 100 µV measured from peak to peak signal (72). To transform the raw EEG signal into each
frequency band, a mean Fast Fourier Transform (FFT) is applied which converts the data from
the time domain into the frequency domain (68,72). An FFT is a particular type of Discrete
Fourier Transform (DFT) that uses an algorithm with reduced calculations to increase speed and
efficiency for analyzing EEG signals (72). The FFT assumes that the signal is finite, as is the
case with EEG and is separated into periodic signals that are derived from a continuous signal by
sampling at an equal time interval. The FFT decomposes the signal into amplitudes at each
frequency. The amplitude value is squared resulting in the calculation of strength or power in
each frequency band which is known as the power spectrum (65).
The band power can be represented as either absolute or relative. The latter is a representation of the frequency band as a percentage of the total power of the signal and is a better reflection of cortical activity as it is less confounded by electrical activity and scalp thickness (73). Graphical representation of a power spectrum is illustrated in figure 3.2.1 with the frequency domain on the x-axis and voltage on the y-axis. Power spectrum is said to follow a stochastic process characterized by the highest power at lower frequencies which declines with increasing frequencies (72). The power spectrum structure follows a $1/f^\gamma$ pattern, also known as pink noise, where the exponent $\gamma$ is said to represent the steepness of the slope between the inverse relationship of higher frequencies (f) and lower power (74). This $1/f$ function has a temporal correlation such that individual frequencies are not mutually exclusive of one another with the exception of a deviation around 10 Hz (alpha band) which presents as a distinctive peak from the $1/f$ envelope (74,75).

Figure 3.2.1: Graphical representation of an EEG power spectrum (76).
Brain waves have been distinguished by their different frequency bands and range from low to high, consisting of delta (0-3 Hz), theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz) and gamma (>30 Hz) (see figure 3.2.2). Each frequency band represents different brain activity and can be categorized as:

Delta: Characterized by the greatest amplitude and slowest frequency and primarily associated with deep non-REM sleep, also known as slow-wave sleep. Since sleep is associated with memory consolidation, delta frequencies play a key role in memory, skill acquisition and learned information (77). Delta waves are stronger in the right hemisphere and sources are typically localized to the thalamus (78).

Theta: Associated with memory recall, information uptake, processing, and learning. Theta waves are generated throughout the cortex and serve as a carrier frequency for cognitive processing across brain regions that are further apart (79).

Alpha: Reflects relaxation, sensory inhibition and sustained attention (78). Alpha band power has shown to be activated in meditation and biofeedback training with eyes closed and is responsible for visual encoding (80). Alpha power is considered a putative marker for arousal and attention and positively correlates with speed of information processing (81).

Beta: This frequency is commonly generated in the primary motor cortex and is responsible for preplanning motor functions such as executing movements, in particularly fine motor skills such as finger dexterity and focused attention. Beta power increases when we observe movements of other individuals indicating an intricate “mirror neuron system” in our brain (82).

Gamma: Neuronal synchronization of the gamma frequency is associated with directed attention and maintenance of working memory processes. Studies also indicate amplification of
the gamma frequency with selective attention involving the somatosensory and auditory systems (83).

Figure 3.2.2: Decomposition of EEG signals into different frequency bands.

### 3.3 EEG Source Analysis

Due to the poor spatial resolution of EEG in comparison to other neuroimaging techniques such as MRI and DTI, it has been difficult to estimate which brain regions generate neuronal activity from the recorded EEG. A fundamental challenge in EEG analysis is solving the inverse problem, i.e., determining the cortical sources that generate an EEG potential on the
scalp. The classic approach to source localization involves dipole sensor-space localization. A dipole is composed of positive and negative charges generated by EPSPs and IPSPs. Negative reflections represent superficial excitatory or deep inhibitory inputs and positive reflections represent deep excitatory or superficial inhibitory inputs (71). Sensor-space localization requires an *a priori* assumption of one or a limited number of active areas in the brain generating the scalp potential field (84). However, a number of problems with sensor-space analysis exist. These include the limited number of scalp electrodes available, the location of the EEG channels do not specifically approximate to the location of underlying neuroanatomy, spurious activity can occur between sensors, and signal leakage from the sensors in the form of field spread and volume conduction can bias results (85,86).

More recent developments in EEG source localization have involved techniques that estimate the dipole magnitude and orientation at fixed positions distributed in the brain. Spherical spline maps estimate the calculation of waveforms at standardized electrode sensor levels (87). The recorded data from the sensor level on the scalp is transformed into a virtual source montage. This creates a 3D map topography generated using all recorded electrodes as well as interpolated *virtual* scalp electrodes allowing for reconstruction of the standard 10-20 or 10-10 coordinate system (87). Visualization and localization of brain activity from cortical sources can then be viewed, thus enhancing the source of the EEG signal (see figure 3.3.1). Several source localization algorithms are available and for a more detailed review of EEG source imaging analysis refer to the review by Michel and colleagues (85). The current study will employ a unique model encompassing both sensor and source-space localization methods for EEG analysis. The latter will include 15 distinctive brain regions to estimate the source of cortical activity.
3.3.1: Illustration of a virtual source montage.

A) Cortical source regions; B) Sagittal view; C) Coronal view; D) 3D view; E) Transverse view.

3.4 EEG Measures in Concussion

EEG is a sensitive measure of neuronal change within the cortex and has been utilized as a modality for identifying potential biomarkers relating to brain function after sustaining a concussion (65). The high temporal resolution of rs-EEG has been shown to quantify alterations in brain function that have extended beyond clinical recovery and symptom resolution (5,7,88). Different computational and analytical methods can be used for EEG such as: connectivity patterns using coherence or symmetry-based metrics, EEG waveform features, event-related potentials (ERPs), source analysis, power spectral density (PSD) and power based analysis (65). The following section will focus on reviewing the concussion literature as it pertains to EEG power based analysis.
Munia and colleagues (89) conducted a rs-EEG longitudinal study comparing healthy controls with SRC athletes at 8, 10 and 12 months post-injury. Results indicate an increase in delta power in concussed athletes compared to controls in frontal brain regions in all three visits. In contrast, beta and gamma power in all brain regions was decreased at 8 and 10 months. Another study by the same authors revealed a similar trend in the subacute stage for 20 concussed adolescent athletes in comparison to healthy age-matched control athletes (90). Increased power was observed in frontal brain regions of delta, theta and alpha frequency bands, with a decrease observed in the beta frequency band. This study included further EEG analysis of individual frequencies for each conventional frequency band which revealed increased power for 3 Hz in delta, 4-5 Hz in theta and 11-12 Hz in alpha. This shift in spectral profile towards lower frequencies may be associated with a maladaptive strategy to lower brain energy demands after sustaining a concussion resulting in cognitive impairments such as attentional and memory deficits (91).

Korn and colleagues (92) conducted a study utilizing quantitative EEG and source analysis and correlated it with single-photon emission computed tomography (SPECT) in a sample of concussed participants experiencing PPCS. Results showed a significant increase in delta power and a decrease in alpha power, with source analysis revealing localization to frontal brain regions. Interestingly an inverse relationship was found with cerebral perfusion and lower EEG frequencies in this study (93). Similar findings concerning increased delta power were reported in a study looking at sleep and concussion (94). Although there was no difference in EEG power during sleep, an increase in delta power and a decrease in alpha power was found upon waking in the concussed group in comparison to controls. A positive correlation was observed between increased delta activity and symptom presentation. The authors conclude with
a statement that increased delta power may be a result of sleep inertia dissipation which might explain symptoms of increased fatigue and ensuing cognitive complaints experienced after concussion. When comparing EEG and MRI, Thatcher and colleagues (95) found damage to white matter tracts to be strongly correlated to an increase in delta amplitude in individuals who sustained a mTBI. White matter axons are reported to be primarily excitatory and diffuse axonal injury sustained from a head injury may reduce this excitatory input therefore resulting in reduced scalp recorded EEG amplitude power in higher frequencies (96).

Conley and colleagues (65) conducted a systematic review of rs-EEG in SRC examining 16 studies and 504 athletes. Six of the studies reported changes in theta power, however, findings were inconsistent for the direction and location of effect with increased and decreased power observed post-concussion. Abnormal theta activity has been associated with a reduction in memory and concentration, increased emotional lability and poor sleep quality. Goal directed attention and decision making have also been implicated with theta oscillations which are important factors when initiating RTP. Although there were less consistent changes observed in other frequency bands, several studies did indicate enhanced delta power and reduced alpha power post-concussion. Furthermore, the authors conclude that studies in the review revealed EEG abnormalities outlasting clinical recovery as measured by neuropsychological measures.

Only two studies to date have investigated exercise and EEG in a concussed cohort. Gay and colleagues (97) conducted an EEG study examining absolute power in a sample of 9 concussed participants and 9 age-matched controls. The concussed group were asymptomatic and cleared for RTP at the time of testing. EEG was measured under four conditions: at rest, during exercise, 30 minutes after exercise and 24 hours after exercise. There was no difference in power at rest or 24 hours after exercise, however, increased power was found during and 30
minutes after exercise between groups. Concussed subjects demonstrated increased average power across delta to beta frequency bands measured in all brain regions in comparison to controls. The largest difference was observed in delta and theta frequencies in occipital brain regions during the exercise condition.

In the second exercise study by Radic and colleagues (98), an increase in theta power after performing an exercise-induced hyperventilation activity was observed in 70 soccer players with a history of mild recurring head injuries compared to healthy controls. An increase in delta power at rest in frontal brain regions was also found in this study. This is in contrast to a study by Devilbiss and colleagues (99), who found a decrease in theta power after performing a 1-mile run in healthy participants. Sex differences contributed to EEG findings, with females presenting with increased delta power and decreased beta power after exercise.

Despite an increase in the amount of studies evaluating functional brain changes in concussion with EEG, there has been conflicting and inconsistent findings reported throughout the literature. This can be attributed to factors such as the heterogeneous nature of concussion, lack of standardized methodological and analytical approaches, sex differences, limited longitudinal data and small and varied sample sizes (65). Further, there is limited research evaluating the effect exercise has on functional brain measures using EEG. However, findings do suggest increased power in lower frequency bands, specifically delta and theta, to be more implicated after sustaining a concussion. This increase is predominately located in frontal and occipital brain regions.
3.5 Extraneous Factors Influencing EEG Measures

Several extraneous factors can also influence EEG findings and thus must be considered, for example EEG power is sensitive to different psychiatric disorders. Newson and Thiagarajan (74) conducted a review of power in EEG frequency bands in conditions such as attention deficit-hyperactivity disorder (ADHD), schizophrenia and obsessive-compulsive disorder and found that there was an increase in absolute power in lower frequencies (delta and theta) with a corresponding decrease across higher frequencies (alpha, beta and gamma). Furthermore, an increased theta/beta ratio is used as a diagnostic biomarker for ADHD in children. Studies evaluating major depressive disorder and rs-EEG using source localization have identified increased theta activity in frontal brain regions such as the anterior cingulate cortex (100). Interestingly, medications such as selective serotonin reuptake inhibitors (SSRIs) have been shown to reverse this trend.

Harrewijn and colleagues (73) found that right frontal cortical activity, as measured via frontal alpha asymmetry, is a putative marker of anxiety and fear avoidance behaviors (73). This is attributed to a reduction in functional coherence between cortical and subcortical brain regions such as the amygdala (101). Chronic pain has also been shown to alter EEG power metrics. Both increases and decreases in different frequency bands reflect the complex spatial-temporal-spectral patterns of the subjective pain experience (102). Increased brain activity at theta frequencies is implicated with chronic pain patients, possibly suggesting abnormal activity between the thalamus and cortex. This may be due to abnormal nociceptive input producing thalamic bursts at theta frequencies that are transmitted to the cerebral cortex (102).
3.6 Aims and Hypotheses

The specific aims of the feasibility study are as follows:

1. To evaluate the feasibility of assessing functional brain changes as measured by EEG spectral power between the concussed and control group before and after performing the BCBT. Specifically, feasibility will be assessed using:
   a) EEG sensor and source-space analysis,
   b) EEG data collection duration,
   c) EEG data quality.

2. To evaluate the feasibility of assessing behavioral measures between the concussed and control group. Specifically, feasibility will be assessed using:
   a) The Buffalo Concussion Bike Test,
   b) The Post-Concussion Symptom Scale,
   c) The Fear-Avoidance after Traumatic Brain Injury Questionnaire,
   d) The Sleep Condition Indicator.

We hypothesize that:

1. It will be feasible to assess functional brain changes using EEG spectral power between the concussed and control group. Specifically:
   a) We expect to see an agreement with the literature of increased EEG spectral power in delta and theta frequencies in frontal brain regions observed in the concussed group compared to the control group pre and post-exertion,
   b) EEG data collection duration for all participants will be less than 60 minutes,
   c) EEG data quality will be acceptable for >80% of all participants.
2. It will be feasible to assess behavioral measures between the concussed group and control group. Specifically, there will be clear group differences when comparing all behavioral measures between the concussed and control group.
Chapter 4: Methodology

4.1 Study Overview

The primary aim of this study was to demonstrate the feasibility of evaluating EEG measures pre and post-exertion in clinically acute to sub-acute concussed participants in comparison to healthy controls. Participants who had sustained a concussion and healthy controls were recruited through word of mouth and flyers (see Appendix A) to the study through the University of British Columbia’s varsity teams, local sports teams and a local concussion and physiotherapy clinic. Each participant underwent behavioral, physiological and electrophysiological assessment over one laboratory session lasting approximately 90 to 120 minutes.

4.1.1 Participants

A total of 10 participants were purposively recruited for this study. This consisted of a group of 5 concussed and 5 control participants recruited from the Greater Vancouver area. All concussed participants were required to meet the following eligibility criteria: aged between 18-35 years, right-handed, a confirmed diagnosis of a concussion within an 8 week period as defined in accordance with the 5th International Conference of Concussion in Sport (Berlin) (4), an onset of PPCS lasting 14 days or more as confirmed through evaluation and a symptom self-report diagnostic checklist. This 14 day period was chosen as previous research demonstrates this period is when over 90% of injured athletes demonstrate recovery on clinical measures (4). Participants were excluded if they presented with evidence of focal neurological deficit, epilepsy, diabetes, heart disease, history of moderate or severe TBI, primary diagnosis of migraine headache or ADHD. The use of prescriptive medications for neurological or psychiatric
conditions was deemed exclusionary, as was an inability to exercise due to orthopedic injury. Control participants were required to conform to the same exclusion criteria and have no prior history of concussion or head injury. All participants provided informed consent, demographic information and past medical history prior to testing (see Appendix B and C).

4.2 Study Procedure

This study employed a between-subjects case-control design. The study received approval from UBC’s Behavioral Research Ethics Board (H19-01156). Participants underwent testing at the Perception-Action Laboratory at the David Mowafaghian Centre for Brain Health at the University of British Columbia. Before entering the study, all participants were required to read the study procedure and provide written consent.

4.2.1 Self-Report Measures

A Physical Activity Readiness Questionnaire (PAR-Q+), the Sleep Condition Indicator (SCI) and the Fear Avoidance Behavior after Traumatic Brain Injury Questionnaire (FAB-TBI) were electronically sent to participants to complete prior to attending the laboratory session (see Appendix D-F). The PAR-Q+ is a questionnaire to evaluate safety to participate in physical activity. The SCI is an eight-item sleep scale that was developed to screen for insomnia. Studies indicate it has sound psychometric properties relating to internal consistency and concurrent validity and a score of ≤16/32 may be indicative of insomnia disorder (104). The FAB-TBI is a 16-item questionnaire evaluating fear avoidance behaviors such as activity and symptom avoidance. The FAB-TBI appears to be a psychometrically sound measure of fear avoidance.
behavior after mTBI (105). Fear avoidance has been associated with physiological deconditioning, ensuing fatigue and concussion like symptoms (106).

Before undertaking EEG recording and exertion testing, participants were required to complete a symptom checklist, followed by balance and vestibular/ocular motor testing. This included the modified Balance Error Scoring System (mBESS) and the Vestibular/Ocular Motor Screening (VOMS). Both the mBESS and the VOMS were administered by a vestibular physiotherapist with clinical experience and certifications in vestibular rehabilitation.

4.2.2 Symptom Scale

After obtaining informed consent, participants were required to complete the Post-Concussion Symptom Scale (PCSS). This symptom checklist consists of a 22-item inventory scale encompassing commonly presented symptoms after sustaining a concussion ranging in severity from 0 (none) to 6 (severe) (see appendix G). Total symptom score and total symptom severity score were calculated pre-exertion for each concussed participant. Symptom severity scores were calculated as the summed total of all reported symptoms. Control participants also completed the PCSS to evaluate symptom presentation. The PCSS has moderate test-retest reliability (0.65) and has a specificity of 91-100% and a sensitivity of 64-89% (48,107).

4.2.3 Modified Balance Error Scoring System

Prior to completing the initial EEG data collection and exercise testing, balance assessment was conducted using the mBESS. The mBESS is a measurement of static balance and postural control that is included in the most recent Sports Concussion Assessment Tool
(SCAT 5) (4). The test involves assuming three different stances. The first stance consists of feet together, the second is a tandem stance with the non-dominant foot in front and the final is a single leg stance on the non-dominant foot. All stances were performed without footwear, with eyes closed and hands resting on hips for a duration of 20 seconds. Potential errors were defined by opening the eyes, lifting the hands off the hips, stepping, falling out of position, lifting the forefoot or heel, abducting the hip by more than 30°, or failing to return to the test position in more than 5 seconds. Errors were calculated in each stance position to produce an overall score. This study incorporated the mBESS which excludes balance on an uneven surface such as a foam cushion. The mBESS has been shown to be reliable and is validated for assessing balance deficits in individuals with a concussion (108).

4.2.4 Vestibular and Ocular Motor Assessment

After completing the mBESS, the Vestibular/Ocular Motor Screening (VOMS) was administered. The VOMS is a screening tool to assess for dysfunction relating to vestibular and ocular motor systems after sustaining a concussion. It consists of 7 domains assessing smooth pursuits, saccadic movements (horizontal and vertical), near point of convergence (NPC), the vestibulo-ocular reflex (VOR) (horizontal and vertical) and motion sensitivity (a copy of the VOMS form and standardized instructions for each test are provided in Appendix H). NPC was measured by asking the participants to focus on a 12-point font letter placed on a tongue depressor that is moved towards the nose at a 20° declined angle. The participant was asked to comment if the font became double or if there was an increase in symptom provocation. The NPC is measured from the tongue depressor to the nose.
Baseline symptoms of headache, dizziness, nausea and fogginess were taken on a Likert scale ranging from 0 (none) to 10 (severe) prior to testing. Participants were then asked to rate the intensity of the 4 symptoms after performing each item on the VOMS on a scale ranging from: no increase (0), mild (+1), moderate (+2) or severe (+3). Testing takes approximately 5-10 minutes to administer. The VOMS demonstrates excellent internal consistency, has concurrent validity correlating positively with the PCSS total symptom score and has been shown to provide good test-retest reliability (109,110). In addition to this, the VOMS may provide a measure of differentiating concussed from non-concussed individuals with cutoff scores of >2 total symptoms after any individual VOMS item or an NPC distance of >5 cm identifying a higher rate of concussion (110).

4.3 Exertion Protocol

After completing the mBESS, VOMS and the initial EEG data collection, the BCBT protocol was conducted. The BCBT is an exertional cycle ergometer test that has been modified from the BCTT. Prior to testing, participants were advised to change into appropriate clothing for exercise and provided with a HR monitor chest strap (Polar H10, Polar Electro Oy, Kempele, Finland). Participants were then informed on what to expect during the BCBT and instructed on the test procedure. Pre-test resting symptoms were recorded on a scale of 0 (none) to 10 (severe) to produce an overall average. The test was deferred if symptoms were > 7/10. Age predicted maximum HR was calculated by subtracting the participants age from 220. This number was then converted to produce 80% of the age predicted maximum HR and used as a criterion for stopping the test. The height of the seat of the cycle ergometer (SportsArt Fitness, model:C535U)
was adjusted to align with the height of the participants anterior superior iliac spine in stance to provide correct biomechanics whilst performing the test.

Participants were instructed to pedal and maintain a rate of $65 \pm 5$ revolutions per minute (RPM) whilst performing the BCBT. After the first minute, resistance was gradually increased every 1 minute for a total duration of 15 minutes. HR (beats per minute), Borg rating of perceived exertion (RPE) (see Appendix I) and symptom severity using a Likert scale of 1-10 were assessed and rated every minute (see Appendix J). Clarification of symptom presentation (i.e. reflection of a new symptom or increased severity of an existing symptom) was noted for the latter. Participants were instructed to report symptoms and to not “push through”. The Borg Scale was placed directly in front of the bike to prevent participants from turning their head during testing. Stopping criteria for the BCBT included: symptom exacerbation which was defined as an increase of 3 points or more from the pre-exercise value (a point or more for an increase in pre-existing symptoms and a point for appearance of a new symptom), RPE exceeding 18, HR reaching 80% of age predicted maximum, participants were deemed unsafe to continue or a request to stop the test was made (110). If the participant violated stopping criteria, HR, RPE and symptom reporting at exercise cessation was recorded. After termination of the test there was a 2-minute cool down with no resistance applied whilst maintaining a speed of 30 RPM.

The BCBT was deemed a more suitable exercise tolerance test for this study as it mitigates the biomechanical forces elicited during the BCTT which may evoke increased cervical and vestibular symptoms not specifically caused by exercise intolerance. A study by Leddy and colleagues has shown that the BCBT is equivalent to the BCTT in respect to HR increase at each stage of testing and HR at symptom exacerbation (111).
4.4 EEG Data Collection

EEG data collection was recorded at two time points: before and immediately after the BCBT. Data was collected using a 64-channel HydroCel Geodesic Sensor Net (EGI, Eugene, OR) arranged according to the international 10-10 system (see figure 4.4.1). EEG was recorded using a Net Amps 300 amplifier at a sampling rate of 500 Hz with a 60 Hz notch filter. Cz was used as the referential electrode. The EEG cap was measured to each participant's head size by calculating the circumference at the glabella to the occipital protuberance and the vertex of the head to the intersection of the periauricular midpoint and nasion-inion midpoint. To increase conductivity, the cap was soaked in a warm water solution containing a mixture of 5 mL of baby shampoo and potassium chloride for 5 minutes prior to application. Scalp impedance was aimed to be less than 5 kΩ. Participants were instructed to sit quietly and relaxed with eyes closed for a duration of 6 minutes. EEG application and setup were approximately 10-15 minutes in duration.
Figure 4.4.1: Locations of electrode placement on the scalp for an EEG (90).

4.4.1 EEG Data Analysis

Data was then analyzed and pre-processed off-line using EEGLAB (http://sccn.ucsd.edu/eeglab; Delorme and Makeig, 2004). An average reference conversion was implemented and filtered from 0.53-50 Hz. Denoising of signal draft, line noise and motion artefacts was applied by removing the EEG signal DC offset. The data derived from the signal processing was then visually inspected and non-neural/stereotypical artefacts were manually rejected. Bad channels displaying large amplitude artifacts were identified and interpolated. An Independent Component Analysis (ICA) linear decomposition was preformed (Runica algorithm,
EEGLAB, with artifactual epochs such as eye movements and myogenic artefacts rejected from further analysis.

In EEGLAB a mean FFT spectrum was applied to EEG signal, transforming the data from time to frequency domain. The output of the FFT was converted to log scale as $10\log(\mu V^2/Hz)$. Individual and within group average power for frequencies ranging from 1-30 Hz was completed in MATLAB (Version R2019b, The Mathworks, Inc., Natick, MA, USA) using a custom script developed in the lab. The script produced an overall average of spectrum activity for each data channel. This study implemented an *a priori* assumption in respect to brain regions of interest (ROI) based on a literature review. If the channel spectra are mapped using EEGLAB, the channel-wise scalp topographies can be observed, and this was visually inspected to identify the presence of activity in the ROI.

Following this, EEG source analysis was processed using the Brain Electrical Source Analysis® software (BESA GmbH, Gräfelfing, Germany). A virtual source montage was applied to the EEG signal to represent cortical activity displaying 15 distinct brain regions. An FFT (1024 segment with 4.10 second overlap) was applied to the virtual source montage to allow for calculation of frequency bands. This study segmented the data into delta (0.5-3 Hz), theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz) and gamma (>30 Hz). This data was then exported to Microsoft Excel (2020) where each frequency band underwent logarithmic transformation from absolute power.

### 4.5 Statistical Analysis

Descriptive statistics was used to describe the demographic characteristics of the participants. Between group comparisons for concussed and control groups were made using
effect size (ES) calculation of Hedge’s g (g) with 95% confidence intervals (CIs) and presented as the mean ± standard deviation. Hedge’s g was chosen as it corrects for upward bias and is recommended in small sample sizes (115). This method of analysis was chosen as feasibility studies are often underpowered, involve small sample sizes and inferential statistical results should be viewed with caution (112–114). Homogeneity of variance was tested using Levene’s test. Results were presented as the median (Mdn) and interquartile range (IQR) when assumptions of normality were violated and for non-parametric data. ES was classified as small (g=0.2), moderate (g=0.5) or large (g=0.8) (115). In cases where homogeneity of variance was violated glasses’ delta (Δ) was calculated (116). For non-parametric data ES was calculated using Cohen statistic \( r (z/\sqrt{N}) \) and interpreted as small (0.1), moderate (0.3) or large (0.5) (117,118). All tests were completed using the statistical software programme Jamovi (version 1.1.3, The Jamovi project, 2020).
Chapter 5: Results

5.1 Participant Characteristics

Seven concussed participants were recruited for this study. However, two of the concussed participants EEG data was unable to be analyzed, therefore this study included five participants in the concussed group and five healthy controls. The concussed group consisted of four females and one male and the control group included two females and three males. Two of the concussed participants had a history of two prior concussions and another had sustained one concussion in the past. No controls had a history of concussion. The MOI for the concussed group consisted of a motor vehicle accident, a fall, a road biking accident whilst commuting, a snowboarding accident and a mountain bike fall. Participants were all right-handed. Participants in the concussed group reported a moderate to high level of activity prior to their concussion, however, frequency and intensity were reported to be considerably decreased post-concussion. One concussion participant had initiated an RTP protocol. Participants characteristics are summarized in table 5.1.1.
Participant characteristics | Concussed | Control |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>22.40 (± 3.78)</td>
<td>23.20 (± 2.95)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>171.00 (± 10.91)</td>
<td>173.40 (± 12.12)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.00 (± 8.60)</td>
<td>69.40 (± 12.78)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n)</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Female (n)</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Time from Injury (days)</td>
<td>37.6 (± 15.9)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Table 5.1.1: Participant characteristics.

5.2 Behavioral Measures

Tables 5.2.1 and 5.2.2 show individual scores and group means for SCI and FAB-TBI measures for concussed and control participants.

For the SCI data the concussed group (Mdn=15.00, IQR=13.00-18.00) reported higher levels of sleep disturbance in comparison to the control group (Mdn=27.00, IQR=26.00-29.00) which produced a large ES; $r=-0.76$. Three participants in the concussed group scored ≤16 which may be indicative of insomnia disorder.

In comparing FAB-TBI scores for the concussed and control group, ordinal data was converted to interval-level measurement properties as suggested by Sneel et al.(105). Results indicate a large ES in the concussed group (24.30 ± 1.99) compared to the control group (3.20 ± 4.59); ($\Delta=4.51$, 95% CI= 15.50-26.70).
<table>
<thead>
<tr>
<th>Participant ID</th>
<th>SCI</th>
<th>Participant ID</th>
<th>SCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCBT_002</td>
<td>18</td>
<td>Control_001</td>
<td>27</td>
</tr>
<tr>
<td>BCBT_003</td>
<td>13*</td>
<td>Control_002</td>
<td>26</td>
</tr>
<tr>
<td>BCBT_004</td>
<td>15*</td>
<td>Control_003</td>
<td>20</td>
</tr>
<tr>
<td>BCBT_005</td>
<td>21</td>
<td>Pilot_001</td>
<td>29</td>
</tr>
<tr>
<td>BCBT_008</td>
<td>13*</td>
<td>Pilot_002</td>
<td>32</td>
</tr>
<tr>
<td>Median</td>
<td>15</td>
<td>Median</td>
<td>27</td>
</tr>
</tbody>
</table>

Table 5.2.1: SCI scores for all participants.

* A score of $\leq 16$ may be indicative of insomnia disorder.

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>FAB-TBI</th>
<th>Participant ID</th>
<th>FAB-TBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCBT_002</td>
<td>24.20</td>
<td>Control_001</td>
<td>0</td>
</tr>
<tr>
<td>BCBT_003</td>
<td>27.16</td>
<td>Control_002</td>
<td>9.94</td>
</tr>
<tr>
<td>BCBT_004</td>
<td>23.66</td>
<td>Control_003</td>
<td>0</td>
</tr>
<tr>
<td>BCBT_005</td>
<td>21.65</td>
<td>Pilot_001</td>
<td>6.05</td>
</tr>
<tr>
<td>BCBT_008</td>
<td>24.77</td>
<td>Pilot_002</td>
<td>0</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>24.29 ($\pm$1.99)</td>
<td>Mean (SD)</td>
<td>3.11 ($\pm$4.59)</td>
</tr>
</tbody>
</table>

Table 5.2.2: FAB-TBI scores for all participants.

5.3 Post-Concussion Symptom Scale

Figures 5.3.1 and 5.3.2 illustrates individual total symptom and total symptom severity scores for concussed and control participants. Figures 5.3.3 and 5.3.4 show the average total symptom and total symptom severity scores for both groups.
For total symptom scores, there was a large ES for the concussed group (12.4 ± 6.23) compared to the control group (0.8 ± 1.30); (Δ=1.86, 95% CI= 3.94-19.30).

For total symptom severity scores, results indicate a large ES increase for the concussed group (41.2 ± 29.5) compared to the control group (0.8 ± 1.30); (Δ=8.92, 95% CI= 3.80-77.0).

The most frequently endorsed individual symptoms reported by the concussed group were headache (3.2%), fatigue (2.6%) and difficulty concentrating (2.6%).
Figure 5.3.1: Concussed and control participants total symptom scores.

Figure 5.3.2: Concussed and control participants total symptom severity scores.
Figure 5.3.3: Concussed and control groups average total symptom scores.

Figure 5.3.4: Concussed and control groups average total symptom severity scores.
5.4 Balance and Vestibular/Ocular Motor Measures

Table 5.4.1 presents individual and mean scores from the mBESS and VOMS for the concussed group. One participant displayed poor balance. Four participants exceeded the clinical cutoff scores of >2 total symptoms after any individual VOMS item and three participants displayed an NPC insufficiency of >5 cm.

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>mBESS</th>
<th>VOMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCBT_002</td>
<td>3 (normal)</td>
<td>6**</td>
</tr>
<tr>
<td>BCBT_003</td>
<td>7 (poor)</td>
<td>11*</td>
</tr>
<tr>
<td>BCBT_004</td>
<td>1 (normal)</td>
<td>17**</td>
</tr>
<tr>
<td>BCBT_005</td>
<td>2 (normal)</td>
<td>0</td>
</tr>
<tr>
<td>BCBT_008</td>
<td>0 (above average)</td>
<td>5**</td>
</tr>
<tr>
<td><strong>Mean ± SD</strong></td>
<td><strong>2.6 ± 2.70</strong></td>
<td><strong>7.8 ± 6.46</strong></td>
</tr>
</tbody>
</table>

Table 5.4.1: VOMS and mBESS scores for the concussed group.

* Exceeds clinical cutoff score.
** NPC insufficiency.

5.5 Exertion Protocol

Tables 5.5.1 and 5.5.2 illustrate the results from the BCBT for the control and concussed group. Only one participant in the concussed group passed the BCBT, with three of the five participants failing due to violating stopping criteria. Three participants exceeded 80% of age predicted maximum HR with one failing at stage 10 and two at stage 6. One concussed participant failed due to +3 symptom exacerbation at stage 9 of the test. In the control group, three participants passed the test whilst two failed at stage 10 due to violating HR criteria. Table 5.5.3 illustrates HR measures for the concussed and control group during the exertion protocol.
<table>
<thead>
<tr>
<th>Participant ID</th>
<th>BCBT Stage (mins)</th>
<th>HR (% max)</th>
<th>RPE</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control_001</td>
<td>15</td>
<td>67%</td>
<td>13</td>
<td>No</td>
</tr>
<tr>
<td>Control_002</td>
<td>10</td>
<td>80%</td>
<td>15</td>
<td>No</td>
</tr>
<tr>
<td>Control_003</td>
<td>15</td>
<td>77%</td>
<td>14</td>
<td>No</td>
</tr>
<tr>
<td>Pilot_001</td>
<td>15</td>
<td>70%</td>
<td>14</td>
<td>No</td>
</tr>
<tr>
<td>Pilot_002</td>
<td>10</td>
<td>80%</td>
<td>14</td>
<td>No</td>
</tr>
</tbody>
</table>

Table 5.5.1: BCBT results for the control group.

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>BCBT Stage (mins)</th>
<th>HR (% max)</th>
<th>RPE</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCBT_002</td>
<td>10</td>
<td>80%</td>
<td>14</td>
<td>+1 Headache</td>
</tr>
<tr>
<td>BCBT_003</td>
<td>9</td>
<td>68%</td>
<td>13</td>
<td>+2 Headache, +1 Dizziness</td>
</tr>
<tr>
<td>BCBT_004</td>
<td>6</td>
<td>80%</td>
<td>13</td>
<td>+1 Headache</td>
</tr>
<tr>
<td>BCBT_005</td>
<td>15</td>
<td>77%</td>
<td>15</td>
<td>+1 Headache</td>
</tr>
<tr>
<td>BCBT_008</td>
<td>6</td>
<td>80%</td>
<td>15</td>
<td>No</td>
</tr>
</tbody>
</table>

Table 5.5.2: BCBT results for the concussed group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Concussed HR (bpm)</th>
<th>Control HR (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise Onset – Stage 1</td>
<td>117.6 ± 18.6</td>
<td>95.7 ± 18.6</td>
</tr>
<tr>
<td>(Mean ± SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum Exercise Tolerance</td>
<td>165.4 ± 21.4</td>
<td>157.3 ± 26.5</td>
</tr>
<tr>
<td>(Mean ± SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall Mean ± SD</td>
<td>135.4± 18.8</td>
<td>126.8± 19.0</td>
</tr>
</tbody>
</table>

Table 5.5.3: Heart rate measures for the exertion protocol.
5.6 EEG Data

For all participants, EEG data collection ranged from 90 to 120 minutes in duration. The majority of EEG data (83%) was acceptable for analysis. However, for two concussed participants, data was unable to be analyzed due to poor quality. This was because of excessive electrode impedance.

5.6.1 Sensor-Space Results

Figures 5.6.1 and 5.6.2 illustrate the PSD for within-group averages for concussed and control groups and each individual participants pre and post-exertion. This data was evaluated qualitatively for within-group differences and represents EEG sensor-space data. On observation there is minimal to no graphical change in average PSD within both groups pre and post-exertion. Figure 5.6.3 compares the PSD between the concussed and control groups pre and post-exertion. There is increased power in the lower frequency range of 1-14 Hz (delta, theta, alpha and low beta) in the concussed groups average pre-exertion in comparison to controls. This pattern is repeated post-exertion. The channel-wise scalp topographies were used to confirm if the brain ROI were more implicated. Red represents enhanced power, whereas blue is reduced power (see figure 5.6.4). For the concussed group, increased spectral power localized to frontal brain regions in 4 Hz (theta) and occipital regions in 6 Hz (theta) was found pre-exertion. Post-exertion revealed increased spectral power in frontal brain regions in 2 Hz (delta) and 4 Hz (theta) for the concussed group compared to the control group.
Figure 5.6.1: Average and individual PSD for control participants pre and post-exertion.
Figure 5.6.2: Average and individual PSD for concussed participants pre and post-exertion.
Figure 5.6.3: Control and concussed groups average PSD.
Figure 5.6.4: Control and concussed groups scalp topographies.
5.6.2 **Source-Space Results**

The following results represents EEG source-space data.

5.6.2.1 **Overall average power between groups pre and post-exertion**

Results indicate a moderate ES was found when comparing pre-exertion overall average power between the concussed (1.93 ± 0.12) and control group (1.81 ± 0.24); ($g$ =0.56, 95% CI= -0.16-0.31).

Post-exertion measures for the concussed (1.84 ± 0.05) and control group (1.77 ± 0.19) revealed a small to moderate ES; ($g$=0.44, 95% CI= -0.14-0.28).

5.6.2.2 **Overall average power within groups pre and post-exertion**

Concussed group: Results indicate a large ES was found when comparing pre-exertion (1.93 ± 0.12) and post-exertion (1.84 ± 0.55) overall average power measures; ($g$=1.07, 95% CI= -0.00-0.19).

Control group: Results indicate a small ES was found when comparing pre-exertion (1.81 ± 0.24) and post-exertion (1.77 ± 0.19) overall average power measures; ($g$=0.32, 95% CI= -0.11-0.19).

5.6.2.3 **Frequency bands**

Whole brain delta frequency band: A large ES was found pre-exertion between the concussed group (Mdn=2.27, IQR=2.25-2.33) and the control group (Mdn=2.09, IQR=2.05-2.13); ($r$=-0.43, 95% CI= -0.24-0.26). Post-exertion revealed a small ES for the concussed group (2.19 ± 0.13) compared to the control group (2.10 ± 0.21); ($g$=0.06, 95% CI= -0.24-0.26).
Whole brain theta frequency band: A small to moderate ES was found pre-exertion for the concussed group (1.98 ± 0.28) compared to the control group (1.86 ± 0.24); (g=0.44, 95% CI= -0.25-0.50). A small to moderate ES was found post-exertion for the concussed group (1.95 ± 0.34) compared to the control group (1.81 ± 0.12); (g=0.46, 95% CI= -0.27-0.55).

Whole brain alpha frequency band: A large ES was found pre-exertion for the concussed group (2.48 ± 0.13) compared to the control group (2.13 ± 0.31); (g=1.30, 95% CI= -0.01-0.69). Post-exertion revealed a large ES for the concussed group (2.48 ± 0.18) compared to the control group (2.15 ± 0.33); (g=1.13, 95% CI= -0.06-0.72).

Whole brain beta frequency band: A small to moderate ES was found pre-exertion for the concussed group (Mdn=1.94, IQR=1.84-1.98) compared to the control group (Mdn=1.83, IQR=1.78-1.85); (r=0.21, 95% CI= -0.23-0.48). Post-exertion revealed a small ES for the concussed group (1.81 ± 0.12) compared to the control group (1.84 ± 0.26); (g=-0.15, 95% CI= -0.32-0.26).

Whole brain gamma frequency band: A small ES was found pre-exertion for the concussed group (0.93 ± 0.36) compared to the control group (0.98 ± 0.26); (g=-0.17, 95% CI= -0.52-0.40). Post-exertion revealed a small ES for the concussed group (0.77 ± 0.46) compared to the control group (0.88 ± 0.25); (g=-0.26, 95% CI= -0.64-0.43).

5.6.2.4 Brain regions

All frequency bands frontal brain regions: A moderate ES was found for the concussed group (1.87 ± 0.15) compared to the control group (1.69 ± 0.27) pre-exertion; (g=0.64, 95% CI= -0.14-0.49). A moderate to large ES was found for the concussed group (1.78 ± 0.13) compared to the control group (1.63 ± 0.23) post-exertion; (g=0.74, 95% CI= -0.12-0.43).
All frequency bands occipital brain regions: A small to moderate ES was found for the concussed group (2.24 ± 0.24) compared to the control group (2.06 ± 0.49) pre-exertion; (g=0.40, 95% CI= -0.39-0.74). A small ES was found for the concussed group (2.00 ± 0.21) compared to the control group (2.10 ± 0.46) post-exertion; (g=-0.26, 95% CI= -0.62-0.42).

Frontal delta frequency: A moderate to large ES was found between concussed (Mdn=2.21, IQR=2.14-2.35) and control (Mdn=2.07, IQR=2.00-2.16) groups pre-exertion; (r=0.36, 95% CI= -0.48-0.55). Post-exertion revealed a small ES between concussed (2.22 ± 0.31) and control (2.23 ± 0.24) groups; (g=-0.02, 95% CI= -0.40-0.39).

Occipital delta frequency: A small ES was found between concussed (2.35 ± 0.31) and control (2.31 ± 0.50) groups pre-exertion; (g=0.08, 95% CI= -0.57-0.65). Post-exertion revealed a small to moderate ES between concussed (2.16 ± 0.28) and control (2.35 ± 0.48) groups; (g=-0.44, 95% CI= -0.77-0.38).

Frontal theta frequency: A moderate to large ES was found between concussed (1.96 ± 0.17) and control (1.77 ± 0.30) groups pre-exertion; (g=0.69, 95% CI= -0.17-0.54). A large ES was found post-exertion between concussed (1.93 ± 0.18) and control (1.68 ± 0.25) groups; (g=1.08, 95% CI= -0.07-0.57).

Occipital theta frequency: A small to moderate ES was found between concussed (2.31 ± 0.41) and control (2.07 ± 0.46) groups pre-exertion; (g=0.44, 95% CI= -0.47-0.94). A small ES was found post-exertion between concussed (2.05 ± 0.52) and control (2.14 ± 0.39) groups; (g=-0.17, 95% CI= -0.76-0.58).

Frontal alpha frequency: A large ES was found for the concussed group (2.17 ± 0.21) compared to the control group (1.83 ± 0.28) pre-exertion; (g=1.24, 95% CI= -0.02-0.70). A large
ES post-exertion was found for the concussed group (2.17 ± 0.12) compared to the control group (1.81 ± 0.36); (Δ=1.00, 95% CI= -0.07-0.81).

Occipital alpha frequency: A large ES was found for the concussed group (3.07 ± 0.33) compared to the control group (2.51 ± 0.62) pre-exertion; (Δ=0.81, 95% CI= -0.21-1.34). A moderate ES was found for the concussed group (2.91 ± 0.31) compared to the control group (2.61 ± 0.53) post-exertion; (Δ=0.56, 95% CI= -0.37-0.96).

Frontal beta frequency: A moderate ES was found for the concussed group (1.87 ± 0.21) compared to the control group (1.74 ± 0.25) pre-exertion; (g=0.52, 95% CI= -0.20-0.47). A small to moderate ES post-exertion was found for the concussed group (1.72 ± 0.19) compared to the control group (1.62 ± 0.34); (Δ=0.29, 95% CI= -0.21-0.50).

Occipital beta frequency: A small to moderate ES was found for the concussed group (2.26 ± 0.18) compared to the control group (2.15 ± 0.51) pre-exertion; (g=0.27, 95% CI= -0.44-0.67). A moderate ES post-exertion was found for the concussed group (1.99 ± 0.12) compared to the control group (2.23 ± 0.45); (g=-0.64, 95% CI= -0.71-0.25).

Frontal gamma frequency: A small ES was found for the concussed group (0.98 ± 0.51) compared to the control group (0.89 ± 0.21) pre-exertion; (g =0.11, 95% CI= -0.52-0.70). A small ES post-exertion was found for the concussed group (0.79 ± 0.55) compared to the control group (0.79 ± 0.18); (g=0.01, 95% CI= -0.61-0.59).

Occipital gamma frequency: A small ES was found for the concussed group (1.19 ± 0.52) compared to control group (1.27 ± 0.46) pre-exertion; (g =-0.16, 95% CI= -0.81-0.63). A small to moderate ES post-exertion was found for the concussed group (0.89 ± 0.45) compared to the control group (1.17 ± 0.69); (g=-0.44, 95% CI= -1.14, 0.57).
Chapter 6: Discussion

The current study aimed to evaluate the feasibility of assessing changes in brain function as measured by EEG in a group of concussed participants in comparison to healthy controls before and after performing the BCBT, a clinical exertion test for concussion. A secondary aim was to evaluate the feasibility of assessing behavioral measures between the concussed and control groups. Findings from the study indicate the feasibility of EEG as a measurement of brain function following a concussion before and after performing the BCBT and the feasibility of assessing behavioral differences between both groups.

6.1 EEG Feasibility

There has been an increase in technological and analytical advancements in measuring functional brain activity in recent years and this has led to an improved understanding of how the brain functions after sustaining a concussion. Current guidelines for concussion diagnosis and treatment consist of a multimodal approach involving a clinically orientated interdisciplinary perspective. However, neurophysiological abnormalities in concussion have been shown to persist beyond the point of clinical recovery and asymptomatic status does not equate to brain recovery (1,4,5,7,88). Conventional neuroimaging techniques are routinely excluded except in cases where moderate to severe forms of TBI are suspected. There is also a paucity of research exploring functional brain changes as measured by EEG in response to exercise using commonly administered clinical tests such as the BCBT. Therefore, to improve our understanding of recovery and prognosis following a concussion, diagnostic biomarkers utilizing novel neuroimaging techniques such as EEG may provide a more accurate assessment of brain function as it relates to aerobic exercise following a concussion.
Results from the feasibility study indicate several interesting findings that will now be discussed. Based on the literature from previous concussion studies using EEG as a measure of brain function, we hypothesized that increased spectral power relating to delta and theta frequency bands in frontal brain regions would be observed in concussed participants before and after performing the BCBT in comparison to healthy controls. We also hypothesized EEG data collection duration for all participants would be less than 60 minutes and data quality would be acceptable for >80% of all participants. The length of time to set-up the protocol was longer than expected, ranging from 90 to 120 minutes for all participants. The increased time duration may have been associated with the EEG cap application taking 10 to 15 minutes to complete pre and post-exertion. It was anticipated that this would require less time. EEG data quality was not acceptable for two concussed participants and this subsequently led to an inability to analyze the data. This was due to high electrode impedance which reduced the signal-to-noise ratio. The increased impedance may have occurred due to excessive sweat on the scalp produced post-exertion. The EEG testing room was poorly ventilated which could have influenced the increased impedance also. Despite this, our study showed the majority of the data was of high quality (83%) and acceptable for analysis thus demonstrating its feasibility.

To our knowledge, this study was the first to evaluate functional brain changes in concussion pre and post-exertion using EEG spectral power with both sensor and source-space analysis. These methods were employed to confirm if power changes in the hypothesized frontal brain regions were present using sensor-space analysis and then provide a more in-depth analytic approach using source-space analysis. EEG source-space analysis is undertaken when evaluating complex EEG measures such as functional connectivity, however, it is not routinely implemented when evaluating EEG spectral power, as sensor space analysis is the preferred
method (85). The former has been shown to more accurately identify the underlying cortical regions responsible for brain activity in comparison to sensor-space analysis, which is limited by spurious estimations of brain regions due to volume conduction and field spread (86).

In the current study, sensor-space analysis using the channel-wise scalp topographies was used to confirm if frontal brain regions were more implicated following a concussion and to graphically identify specific frequencies of increased EEG power. Findings included increased spectral power in 1-14 Hz (delta, theta, alpha and low beta frequencies) in the concussed group compared to controls pre and post-exertion and increased power in frontal brain regions of the 2 Hz and 4 Hz (delta and theta frequencies) post-exertion (see figures 5.6.3 and 5.6.4). Source-space analysis revealed a large effect for frontal theta and alpha power when comparing the concussed and control groups pre and post-exertion EEG measures. A prominent increase in EEG power was found in frontal brain regions of the theta frequency band with a mean difference of 0.25±0.14. This demonstrated a large effect post-exertion (ES=1.08 SD; 95% CI=-0.07-0.57; power=46%). Less prominent findings were observed in the hypothesized delta frequency, however, a large effect was found for alpha power pre-exertion in the concussed group compared to controls (ES=1.24 SD; 95% CI=-0.02-0.70; power=58%). A large effect was also found in all frequency bands in frontal brain regions in the concussed group compared to controls post-exertion (ES=0.74 SD; 95%CI=0.12-0.43; power=25%).

These results are consistent with previous research investigating exercise and EEG in concussion where increased frontal theta power was reported relative to pre-injury measures or in comparison to controls during and after performing an exertion protocol (97,98). Furthermore, findings from 71 individuals diagnosed with military-related mTBIs revealed atypical increases in theta power in comparison to controls using a multivariate approach to predict mTBI
classification (119). Conley and colleagues (65) reported similar findings in a systematic review on rs-EEG in SRC where abnormal theta rhythms were observed in 6 of the 16 studies reviewed. Frontal theta power has been reported to positively correlate with exercise intensity in young healthy participants performing a cycle ergometer test (120). However, as target HR approximates 60% to 70% of maximum threshold, theta power decreases, possibly suggesting increased neural efficiency due to a shift of neural activity to other frequencies.

It could be inferred that moderate-to-high aerobic exercise induces an increased investment of neural demand that the concussed brain is unable to adapt to. This may then present as an increase in the neural load of the theta frequency band in frontal brain regions as a maladaptive strategy for this augmented workload. However, future research utilizing EEG during the exertion protocol and involving a larger sample size and statistical power would need to be performed to confirm this. In addition, studies indicate exercise-induced brain wave activity returns to resting level state within 30 minutes after exercise cessation (121,122). This may have reduced the sensitivity of observing more pronounced within-group changes post-exercise in both groups. Despite this, source-space results did indicate a large effect was found for a reduction in average power within the concussed groups pre and post-exercise values (ES=1.07 SD; 95% CI= -0.00-0.19). However, due to the majority of participants not passing the BCBT, the true extent the test has on EEG power remains in question.

Increased activity in theta and alpha wave spectrums may also be indicative of fatigue. Tran and colleagues (123) conducted a systematic review with meta-analysis of 21 studies of EEG spectral activity and mental fatigue. Results indicate a large increase in theta activity (ES =1.24 SD; 95% CI= 0.44–1.95) in frontal brain regions, with the authors concluding that this neural signature is a definite and valid biomarker of mental fatigue. Alpha oscillations were also
found to be moderately increased in frontal regions (ES =0.50 SD; 95% CI= −0.46–1.36). Baseline PCSS scores indicated fatigue as a prominent symptom contributor for the concussed group which would be expected to increase after performing a vigorous exercise task. In conjunction with this, decreased exercise tolerance due to physiological deconditioning post-concussion may have significantly influenced performance decrement observed during the BCBT. Concussed participants reported attenuated physical activity levels post-injury with only one participant engaged in a monitored RTP protocol. This reduction in exertional capacity could reflect the observed increase in the 1-14 frequency range as a result of fatigue. However, it is unclear if fatigue was mediated from central or peripheral mechanisms. The latter would be speculated to reflect increased alpha power post-exercise when muscle relaxation is initiated (122).

Another factor contributing to an increase in lower frequency band power is altered cerebral perfusion. For example, O’Gorman and colleagues (124) examined coupling between EEG oscillations and cerebral perfusion using arterial spin labeling and found a negative correlation between delta and theta frequency bands and perfusion levels. Autonomic dysregulation and alterations in CBF are a common characteristic experienced post-concussion and have been associated with symptom presentation and exercise intolerance (39–41,111). Cerebral hypoperfusion may have contributed to this low-frequency neural increase observed in 2 Hz and 4 Hz in frontal brain regions on the topographical maps of the concussed group post-exertion. However only one of the concussed participants had a symptom-limited response to the BCBT which would disprove ANS dysfunction as the causative factor.

A more plausible rationale for test failure may be physiological deconditioning, as the majority of the concussed group failed due to HR criteria. The BCBT is an exertional test that
has been developed to assess exercise tolerance in an athletic population which was not representative of participants in the concussed group. Furthermore, two participants in the control group failed due to violating HR criteria. Interestingly all participants who failed due to HR criteria were female. This may justify deconditioning as the reason for test failure as females have been shown to present with lower peak VO₂ in comparison to males in response to maximal exercise stress tests (125).

6.2 Behavioral Measures

Despite the substantial amount of variability in the concussed groups demographics such as mechanism of injury and time since injury, clear group differences were observed when comparing the two groups. The concussed group reported a reduction in sleep quality as indicated by SCI scores with three participants reporting ratings suggestive of insomnia disorder. Sleep-wake disturbances negatively impact recovery by increasing PPCS such as fatigue, anxiety, irritability and cognitive function (126). For example, athletes performed worse on CNTs when sleep was less than 7 hours prior to testing (127). Neurophysiological findings of cortical hyperarousal are present in individuals with insomnia and are typically characterized by increased power at lower frequency bandwidths, this may have contributed to the presence of increased power in the concussed group (128). Furthermore, poor sleep quality could have resulted in the prominent increase in levels of fatigue reported in the concussed group. However, a study by Gosselin and colleagues (94) reported no objective differences in sleep characteristics using polysomnography when comparing concussed and control athletes despite subjective sleep complaints from the former. In the same study, an increase in delta power was observed upon
waking which may be indicative of slower sleep inertia disputation leading to subjective
dyssomnina and fatigue.

Our results indicate VOMS scores exceeded the clinical cut-off threshold for four of the
concussed participants. Convergence insufficiency (near point of convergence >5cm) was also
found in three concussed participants and has been associated with prolonged recovery by 12.3-folds after sustaining a concussion (129). Leddy and colleagues (14) have suggested distinct
concussive subtype presentations as elucidated from clinical history, physical examination and
exertion testing using the BCTT or BCBT. Findings from the current study may indicate that
concussed participants presented with vestibular/ocular motor dysfunction rather than
physiological impairment which resulted in a protraction in recovery. This may have also
reflected the high subjective reports of headache, fatigue and difficulty concentrating which is
commonly seen when vestibular and ocular motor function is impaired (130,131).

Fear avoidance scores were reported to be significantly higher in the concussed group
compared to controls (ES=4.51 SD; 95% CI= 15.50-26.70). This is indicative of increased levels
of activity and symptom avoidance and cogniphobia. The latter is reflective of avoidance of
mental tasks due to fear of exacerbating symptoms and may have been indicative of the
concussed group's high report of headaches (105). Although an initial period of rest is advised
after sustaining a concussion, limiting movements due to maladaptive coping strategies can lead
to physical deconditioning as soon as 3 days post-injury and has been associated with a
protracted recovery time especially after the acute stage (45). Fear of exacerbating symptoms due
to movement which is also known as kinesiophobia is associated with vestibular dysfunction due
to reduced habituation to provocative movements (44). This may have contributed to decreased
activity levels and physiological deconditioning in the concussed group. Additionally, high
levels of avoidance behavior and disengagement of valued activities are associated with anxiety, which is a prognostic factor for the development of PPCS and a protraction in recovery time (45). A caveat worth noting from a systematic review examining EEG and anxiety found increased power across lower frequency bands which may have confounded results in the current study (74). Furthermore, frontal brain regions are known to be involved in emotional processing (132). Due to the complex nature of concussion, a biopsychosocial approach is paramount to enhance activity level outcomes.

### 6.3 Strengths, Limitations and Future Directions

The concussed participants consisted of a heterogeneous sample that varied in age (18 to 28 years) and sustained their concussions from various mechanisms of injury and at different timeframes. Recruitment of the concussed participants was difficult, which may have implications for future studies, therefore additional recruitment methods should be considered. Sex differences may have contributed to findings as the majority of the concussed group were female. In the most recent CISG consensus statement, females reported higher symptom presentation and are more susceptibility to a protracted recovery (4). This may be due to a number of reasons such as physical and physiological differences such as neck strength and hormonal influences.

There was also considerable variability in respect to pre and post-injury physical fitness levels. The BCBT has been developed to test concussed athletes exercise tolerance and facilitate a more objective approach for RTP. This was not representative of the current studies participants, who present with varied backgrounds of aerobic conditioning. Future studies employing a moderate exertional protocol for a longer timeframe may distinguish more
pronounced cortical activation patterns. Interestingly, the only concussed participant to pass the BCBT was a keen mountain biker and it could be inferred she was more physiologically adapted to complete the BCBT in comparison to the other participants. This participant also reported the longest time period since injury and therefore had the longest recovery time which could have influenced results. The BCBT may therefore be more suitable in the sub-acute stage post-concussion for the non-athlete population.

There was a lack of blinding when administering the behavioral measures by the research investigator which can lead to confirmation and performance bias (133). Future studies should incorporate a blinded protocol to mitigate this. Furthermore, VOMS and mBESS were administered exclusively on the concussed group to screen for vestibular/ocular motor dysfunction which may have altered pre-exertion EEG power. However, this timeframe was chosen as previous research has demonstrated significant increases in total VOMS and NPC scores following exertional fatigue (134).

Although the current study employed a source analysis method, EEG has low spatial resolution with the main signal source originating from the cerebral cortex. This lack of anatomical specificity prevents deeper cortical analysis which is often implicated in concussion. For example, exercise-induced arousal is said to stem from the reticular activating center which correlates with the activation of individual alpha peak frequency and CBF (81). DTI studies have also found regions in the brain stem to be more effected after a concussion (135). Advanced methods of analysis such as coherence and functional connectivity measures exploring different brain regions, frequency bands, and cerebral hemispheres would provide a more in-depth approach of brain function for future studies. Additionally, EEG measurements taken pre-injury and longitudinal data involving an intermediate time point would provide a more reliable picture
of the neurophysiological changes that are present post-concussion. There are also pre-existing confounding factors such as emotional status, caffeine intake and diurnal effects that can influence EEG results and thus need to be considered.
Chapter 7: Conclusion

The current study is supported by accumulating evidence of concussed individuals acquiring an increase in cortical resources in comparison to pre-injury measures or healthy controls. Results indicate that this is putatively present before and after performing the BCBT as measured by EEG spectral power using sensor and source-space analysis. Although data collection duration was longer than anticipated, EEG quality was acceptable for the majority of participants thus demonstrating its feasibility for assessing brain function in concomitant with behavioral measures. Furthermore, clear group differences were demonstrated on behavioral measures. The utility of EEG as a portable, non-invasive, time and cost-efficient modality for assessing functional brain changes could potentially provide a more robust indicator of recovery following a concussion in the future. The applicability of EEG to mainstream clinical use for concussion diagnosis, prognosis and management warrants further investigation involving a larger dataset for comparison of normative and non-normative classification values. Used in conjunction with a multifaceted approach involving clinical measures may provide increased sensitivity and specificity for the detection of concussive defects and more accurate and informed RTP decisions.
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Appendices

Appendix A

Advertisement to Recruit Participants

UBC UNIVERSITY OF BRITISH COLUMBIA

Concussion Research Study

The Study of Exercise in Concussion

aims to find out the changes in brain activity with exercise after sustaining a concussion.

**Eligibility:** We are looking for adults between the ages of 18-35 who are **one-to-eight weeks post-concussion**

**Description:** We will be measuring brain activity pre and post exercise using EEG lasting approximately one hour.

**Location:** The study will take place at UBC Centre for Brain Health under the principal investigator of Dr Naznin Virji-Babul.

**Reimbursement:** You will receive financial compensation for your participation.
Appendix B  Consent Form

The University of British Columbia
Faculty of Medicine
Department of Physical Therapy
Vancouver Campus
212-2177 Wesbrook Mall
Vancouver, BC, Canada, V6T 1Z3

Exploring the Neurophysiological Effects of Aerobic Exercise in Concussion. An Exploratory Electroencephalography Study.

Informed Consent

1. Investigators Conducting the Study

   Principal Investigator: Naznin Virji-Babul, PT, PhD, Department of Physical Therapy, Faculty of Medicine

   Study Team Members: Patrick O’ Flaherty, BSc (Hons) PT, Rehabilitation Sciences UBC.

   Co-Investigators: Dr. William Panenka
                    Dr. Noah Silverberg

2. Source of Support

   There is no outside funding for this study.

3. Invitation to Participate

   You are being invited to participate in this research study to help identify the changes in brain activity in a concussed population during a graded exercise protocol. The purpose of the research is to study the effects aerobic exercise has on brain activity with participants experiencing post-concussion symptoms. Findings from this research will allow for quantification of brain network connectivity to help identify potential biomarkers in participants who have experienced a concussion.
4. Participation is Voluntary

Participation is entirely voluntary, it is up to you to decide if you want to participate in this study or not. Before you decide, it is important for you to decide what the research involves. This consent form will tell you about the study, why the research is being done, what will happen to you during the study and the possible benefits, risks and discomforts,

If you wish to participate, you will be asked to sign this form. If you decide to take part in this study, you are still free to withdraw at any time and without giving any reason from your withdrawal.

Data from the study will be publicly accessible in the future and your personal information such as name, age etc will not be identified. This has the potential to increase participant risk and once the data is made publicly available, you will not be able to withdraw your data.

If you do not wish to participate, you do not have to provide any reason for your decision not to participate nor will you lose the benefit of any medical care to which you are entitled and currently receiving.

Please take your time to read the following information carefully and to discuss it with your family, friends, and doctor before you decide.

5. Purpose

The purpose of this study is to characterize brain activity in adults who are experiencing symptoms after sustaining a concussion after completing exercise. This will be done using electroencephalography (EEG). The results from this study will help us understand how concussion during sports can affect the function of the brain.

6. Who Can Participate in this Study?

We are aiming to recruit 15 right handed participants who have had a concussion within 8 weeks between the ages of 18-35 years of age with an onset of post-concussion symptoms lasting more than 8 days.

7. Who Should Not Participate in this Study?

You should not participate in this study if you have a history of seizure, epilepsy, neurodegenerative disorder, major head trauma or other neurological conditions, diabetes or known heart disease, primary diagnosis of migraine headaches, in ability to exercise due to orthopaedic injury, history of attention deficit disorder, prescription medication for neurological or psychiatric conditions, a past medical
history of fear avoidance behaviour or premorbid anxiety and depression, drug or alcohol abuse or inability to understand English.

8. What Does the Study Involve?
If you are eligible and decide to participate in this study, you will come to the Perception-Action Lab (3450 Mowafaghian Centre for Brain Health, UBC) on one occasion lasting for 1 hour.

Your participation will involve the following:

1) Sport Concussion Assessment Tool (SCAT) 5th Edition: The SCAT 5 is a standardised tool used my medical professionals and qualified healthcare professionals to aid in the evaluation of athletes suspected of having sustained a concussion. The SCAT 5 has two major components, an immediate on file assessment tool and an off-field assessment tool. The immediate on field assessment tool comprises of taking note of red flags, checking for observable signs of concussion, memory assessment using Maddocks questionnaire, examining the level of consciousness using the Glasgow Coma Scale and cervical spine assessment.

The off-field assessment comprises of taking a comprehensive history of the players condition, symptom evaluation, a cognitive screen, which is a measure of orientation and immediate memory, a measure of concentration, a neurological screen and delayed recall.

2) Vestibular/Ocular Motor Screening (VOMS): The VOMS is a screening tool developed detect signs and symptoms of a concussion. It looks at the systems responsible for integrating balance, vision and movement. The screening test for five areas of vestibular and oculomotor impairment consisting of smooth pursuits, saccadic or rapid eye movements, near point of convergence, vestibular ocular reflex and visual motion sensitivity.

3) Questionnaires:
   - Post-Concussion Symptom Scale: The Post-Concussion Symptom Scale (PCSS) is a 22-item inventory scale of 0 (none) to 6 (severe encompassing commonly presented symptoms after sustaining a sports related concussion.
   - Anxiety and Depression Questionnaire: PROMIS (Patient-Reported Outcomes Measurement Information System) is a set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children.
   - Fear Avoidance Questionnaire: The Fear Avoidance Behavior in Traumatic Brain Injury questionnaire (FAB-TBI) has 16 items with Likert scale response options. The FAB-TBI was developed by factor analyses of existing fear avoidance measures from the chronic pain literature.
   - Sleep Condition Indicator (SCI): The SCI is valid, reliable and sensitive to change in insomnia severity. Its brevity and appealing
visual format permit rapid assessment and interpretation of poor sleep against contemporary clinical diagnostic criteria.

- PAR-Q: Participants will be required to complete a PAR-Q at baseline assessment, if yes has been indicated in answering the they will be required to visit their family physician and obtain clearance for exercise testing."

4) Resting State EEG Scan

An Electroencephalogram (EEG) is a technique for studying the electrical current within the brain. Electrodes are attached to the scalp. Wires attach these electrodes to a machine which records the electrical impulses. The results are either printed out or displayed on a computer screen. You will not be able to use hair products before coming in for your appointment, this includes conditioner, mousse, hairspray, etc. Shampoo is fine. You will be asked to sit quietly as possible with eyes closed for 5 minutes pre and post exercise exertion task.

5) Exercise Exertion Task

You will be asked to put on the Polar Heart Rate monitor and sit on a recumbent bicycle. You will be performing the Buffalo Concussion Bike Test (BCBT). The BCBT involves beginning cycling at 60 revolutions per minute with the resistance increased every 1 minute for a total duration of 15 minutes. Heart rate (HR), the rating of perceived exertion (RPE-Borg scale of 6-20) and symptom increase using a likert scale (0-10) will be monitored at baseline and will be assessed every minute (6). Blood pressure (BP) is also measured pre exertion. The test will be stopped if symptom exacerbation occurs (>3-point change in symptom score), RPE reaches >17, HR reaches 90% of age predicted max, you are deemed unsafe to continue or a request to stop the test is made. After termination of the test a final set of values for BP and HR will be taken.

9. What Are Possible Harms and Side-Effects of Participation?
The risks are not greater than the risks in everyday life. Collection of EEG data involves the placement of surface electrodes on your skin. This allows for the detection of brain signals. You will feel little or no discomfort during the EEG. The EEG only records brain waves and will not transmit any sensations.
You will be asked to compete an exercise session lasting approximately 15 minutes on a stationary bicycle. You will also be wearing a heart rate monitor. There is a possibility of the return of symptoms during exercise for individuals with post-concussion symptoms. Should this occur, the current exercise session will be immediately stopped. As with all exercise training programs there are associated risks of injury such as falling off the bike; you may also become very tired, experience muscle soreness, and discomfort common to starting an exercise program. Although unlikely in a healthy, athletic population, we will attempt to avoid these risks through close monitoring by the researchers.

10. What are the Benefits to You of Participating in the Study?
There is no direct benefit to you for participating in this study. It is hoped that information gained in this research study may be useful in understanding the impact of concussion on brain function.

11. Confidentiality:
Your confidentiality will be respected. No information that discloses your identity will be released or published without your specific consent to the disclosure. However, research records and medical records identifying you may be inspected in the presence of the Investigator or his or her designate and the UBC Clinical Research Ethics Board for the purpose of monitoring the research. However, no records which identify you by name or initials will be allowed to leave the Investigators' offices.

All study data will initially be collected either on paper or on the computer (if it is one of the computerized tests). All paper forms will be kept in a locked drawer in a locked room at UBC separate from consent forms.

Electronic data and the devices used to store data (laptops, USB's, etc) will be password protected and encrypted.

You will be assigned a unique study number as a participant in this study. This number will not include any personal information that could identify you (e.g., it will not include your Personal Health Number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during the course of this study, so that your identity will be kept confidential. Information that contains your identity will remain only with the Principal Investigator and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.
Your participation in this study is voluntary and you may withdraw at any time. You do not need to provide a reason for your withdrawal. The data we collect up to the point of your withdrawal from the study will be kept for data analysis purposes under strict provisions of confidentiality.

By signing this form, you do not give up any of your legal rights and you do not release the study investigator or other participating institutions from their legal and professional duties. There will be no costs to you for participation in this study. You will not be charged for any research procedures.

12. Contact for information about the study:
If you have any questions or desire further information with respect to this study, you may contact Dr. Naznin Virji-Babul
Consent to Participate

Exploring the Neurophysiological Effects of Aerobic Exercise in Sports-Related Concussion. An Exploratory Electroencephalography Study.

- I have read and understood the subject information and consent form.
- I have been told that I will receive a dated and signed copy of this form.
- I have had sufficient time to consider the information provided and to ask for advice if necessary.
- I have had the chance to ask questions and have received satisfactory answers.
- I understand all of the information collected will be kept confidential, and that the results will only be used for scientific objectives.
- I understand that my participation in this study is voluntary and that I am completely free to refuse to participate or to withdraw from this study at any time.
- I understand that I am not waiving any of my legal rights as a result of signing this consent from.
- I understand that this study will not provide any direct benefit to me.
- I have read this form and I freely consent to take part in this study.

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My signature above signifies that the study has been reviewed has been received with the participant by me and/or by my delegated staff. My signature may have been added at a later date, as I may not have been present at the time the participant’s signature was obtained.
Appendix C  Demographic Information and Past Medical History

Demographic Information

Section I: Demographic Information

Name:

Height:

Weight:

Date of Birth:

Age:

Section II: Concussion History

<table>
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<tr>
<th>Date of concussion (dd/mm/yyyy)</th>
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<td>Did the concussion occur while participating in sport?</td>
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<tr>
<td>Which sport did you sustain your concussion in?</td>
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<tr>
<td>If no please state how you sustained your concussion.</td>
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<td>Check the box if your concussion resulted in:</td>
<td>□ Loss of consciousness □ Trouble remembering □ Dizziness □ Confusion</td>
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Please describe the current symptoms you are experiencing:

Have you continued to exercise since your injury?

What was your level of exercise prior to your concussion? Please details frequency, intensity and duration.

How many concussions have you had in the past? Please list and date.

Section III: General Medical History.

Please check off any of the conditions below that you have been diagnosed with.

☐ Development delay ☐ Autism ☐ Anxiety ☐ Post-Traumatic Stress Disorder ☐ Motion Sickness (ex. Car or plane rides) ☐ Hypertension ☐ Neck Problems ☐ Hearing Problems ☐ Osteoporosis ☐ Gastrointestinal ailments ☐ Seizures ☐ Currently Pregnant ☐ Learning disability ☐ Attention deficit hyperactivity disorder (ADHD) ☐ Obsessive-Compulsive Disorder ☐ Headaches ☐ Diabetes ☐ Respiratory/Pulmonary problems (asthma, COPD) ☐ Sleep Apnea ☐ Meningitis ☐ Fine Motor Difficulties ☐ Speech/Language Disorder ☐ Complex regional pain syndrome ☐ Dyslexia ☐ Depression ☐ Bipolar Disorder ☐ Migraines ☐ Heart Disease ☐ Back problems ☐ Visual Problems ☐ Osteo/Rheumatoid Arthritis ☐ Cancer or tumors ☐ Neurological Disorder (MS, stroke, paralysis) ☐ HIV/AIDS

Past Surgical History/Imaging or Scans of the head and neck (include procedure, date and surgeon/hospital):

Current Medications:
Appendix D  PAR-Q+

2019 PAR-Q+
The Physical Activity Readiness Questionnaire for Everyone

The health benefits of regular physical activity are clear; more people should engage in physical activity every day of the week. Participating in physical activity is very safe for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor or a qualified exercise professional before becoming more physically active.

**GENERAL HEALTH QUESTIONS**

<table>
<thead>
<tr>
<th>Question</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Has your doctor ever said that you have a heart condition OR high blood pressure?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2) Do you feel pain in your chest at rest, during your daily activities of living, OR when you do physical activity?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) Do you lose balance because of dizziness OR have you lost consciousness in the last 12 months? Please answer NO if your dizziness was associated with over-breathing (including during vigorous exercise).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4) Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)? PLEASE LIST CONDITION(S) HERE:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5) Are you currently taking prescribed medications for a chronic medical condition? PLEASE LIST CONDITION(S) AND MEDICATIONS HERE:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6) Do you currently have (or have had within the past 12 months) a bone, joint, or soft tissue (muscle, ligament, or tendon) problem that could be made worse by becoming more physically active? Please answer NO if you had a problem in the past, but it does not limit your current ability to be physically active. PLEASE LIST CONDITION(S) HERE:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7) Has your doctor ever said that you should only do medically supervised physical activity?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If you answered NO to all of the questions above, you are cleared for physical activity. Please sign the PARTICIPANT DECLARATION. You do not need to complete Pages 2 and 3.

- Start becoming much more physically active - start slowly and build up gradually.
- Follow international Physical Activity Guidelines for your age (www.who.int/dietphysicalactivity/en/).
- You may take part in a health and fitness appraisal.
- If you are over the age of 45 yr and NOT accustomed to regular vigorous to maximal effort exercise, consult a qualified exercise professional before engaging in this intensity of exercise.
- If you have any further questions, contact a qualified exercise professional.

**PARTICIPANT DECLARATION**

If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that the community/fitness center may retain a copy of this form for its records. In these instances, it will maintain the confidentiality of the same, complying with applicable law.

NAME ___________________________ DATE ___________________________
SIGNATURE ___________________________ WITNESS ___________________________
SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER ___________________________

If you answered YES to one or more of the questions above, COMPLETE PAGES 2 AND 3.

⚠️ Delay becoming more active if:

- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the epARmed-X at www.eparmed.com before becoming more physically active.
- Your health changes - answer the questions on Pages 2 and 3 of this document and/or talk to your doctor or a qualified exercise professional before continuing with any physical activity program.
<table>
<thead>
<tr>
<th>1. <strong>Do you have Arthritis, Osteoporosis, or Back Problems?</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>If the above condition(s) is/are present, answer questions 1a-1c if <strong>NO</strong> go to question 2</td>
<td></td>
</tr>
<tr>
<td>1a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer <strong>NO</strong> if you are not currently taking medications or other treatments)</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>1b. Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/or spondyloysis pars defect (a crack in the bony ring on the back of the spinal column)?</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>1c. Have you had steroid injections or taken steroid tablets regularly for more than 3 months?</td>
<td><strong>YES</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. <strong>Do you currently have Cancer of any kind?</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>If the above condition(s) is/are present, answer questions 2a-2b if <strong>NO</strong> go to question 3</td>
<td></td>
</tr>
<tr>
<td>2a. Does your cancer diagnosis include any of the following types: lung/brechnogenic, multiple myeloma (cancer of plasma cells), head, and/or neck?</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>2b. Are you currently receiving cancer therapy (such as chemotherapy or radiotherapy)?</td>
<td><strong>YES</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. <strong>Do you have a Heart or Cardiovascular Condition? This includes Coronary Artery Disease, Heart Failure, Diagnosed Abnormality of Heart Rhythm</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>If the above condition(s) is/are present, answer questions 3a-3d if <strong>NO</strong> go to question 4</td>
<td></td>
</tr>
<tr>
<td>3a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer <strong>NO</strong> if you are not currently taking medications or other treatments)</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>3b. Do you have an irregular heart beat that requires medical management? (e.g., atrial fibrillation, premature ventricular contraction)</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>3c. Do you have chronic heart failure?</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>3d. Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?</td>
<td><strong>YES</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. <strong>Do you have High Blood Pressure?</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>If the above condition(s) is/are present, answer questions 4a-4b if <strong>NO</strong> go to question 5</td>
<td></td>
</tr>
<tr>
<td>4a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer <strong>NO</strong> if you are not currently taking medications or other treatments)</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>4b. Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer <strong>YES</strong> if you do not know your resting blood pressure)</td>
<td><strong>YES</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. <strong>Do you have any Metabolic Conditions? This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>If the above condition(s) is/are present, answer questions 5a-5e if <strong>NO</strong> go to question 6</td>
<td></td>
</tr>
<tr>
<td>5a. Do you often have difficulty controlling your blood sugar levels with foods, medications, or other physician-prescribed therapies?</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>5b. Do you often suffer from signs and symptoms of low blood sugar (hypoglycemia) following exercise and/or during activities of daily living? Signs of hypoglycemia may include shakiness, nervousness, unusual irritability, abnormal sweating, dizziness or light-headedness, mental confusion, difficulty speaking, weakness, or sleepiness.</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>5c. Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, OR the sensation in your toes and feet?</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>5d. Do you have other metabolic conditions (such as current pregnancy-related diabetes, chronic kidney disease, or liver problems)?</td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td>5e. Are you planning to engage in what for you is unusually high (or vigorous) intensity exercise in the near future?</td>
<td><strong>YES</strong></td>
</tr>
</tbody>
</table>
### 2019 PAR-Q+

6. **Do you have any Mental Health Problems or Learning Difficulties?** This includes Alzheimer's, Dementia, Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndrome
   
   If the above condition(s) is/are present, answer questions 6a-6b  
   **If NO** go to question 7
   
   6a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies?  
   **(Answer NO if you are not currently taking medications or other treatments)**  
   **YES** NO
   
   6b. Do you have Down Syndrome AND back problems affecting nerves or muscles?  
   **YES** NO
   
7. **Do you have a Respiratory Disease?** This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure
   
   If the above condition(s) is/are present, answer questions 7a-7d  
   **If NO** go to question 8
   
   7a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies?  
   **(Answer NO if you are not currently taking medications or other treatments)**  
   **YES** NO
   
   7b. Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen therapy?  
   **YES** NO
   
   7c. If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough (more than 2 days/week), or have you used your rescue medication more than twice in the last week?  
   **YES** NO
   
   7d. Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?  
   **YES** NO
   
8. **Do you have a Spinal Cord Injury?** This includes Tetraplegia and Paraplegia
   
   If the above condition(s) is/are present, answer questions 8a-8c  
   **If NO** go to question 9
   
   8a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies?  
   **(Answer NO if you are not currently taking medications or other treatments)**  
   **YES** NO
   
   8b. Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?  
   **YES** NO
   
   8c. Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?  
   **YES** NO
   
9. **Have you had a Stroke?** This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event
   
   If the above condition(s) is/are present, answer questions 9a-9c  
   **If NO** go to question 10
   
   9a. Do you have difficulty controlling your condition with medications or other physician-prescribed therapies?  
   **(Answer NO if you are not currently taking medications or other treatments)**  
   **YES** NO
   
   9b. Do you have any impairment in walking or mobility?  
   **YES** NO
   
   9c. Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?  
   **YES** NO
   
10. **Do you have any other medical condition not listed above or do you have two or more medical conditions?**
   
   If you have other medical conditions, answer questions 10a-10c  
   **If NO** read the Page 4 recommendations
   
   10a. Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months **OR** have you had a diagnosed concussion within the last 12 months?  
   **YES** NO
   
   10b. Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?  
   **YES** NO
   
   10c. Do you currently live with two or more medical conditions?  
   **YES** NO

**PLEASE LIST YOUR MEDICAL CONDITION(S) AND ANY RELATED MEDICATIONS HERE:**

---

**GO to Page 4 for recommendations about your current medical condition(s) and sign the PARTICIPANT DECLARATION.**
2019 PAR-Q+

If you answered YES to one or more of the follow-up questions about your medical condition:
You should seek further information before becoming more physically active or engaging in a fitness appraisal. You should complete the specially designed online screening and exercise recommendations program - the ePARmed-X+ at www.eparmed.com and/or visit a qualified exercise professional to work through the ePARmed-X+ and for further information.

Delay becoming more active if:
- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your healthcare practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ at www.eparmed.com before becoming more physically active.
- Your health changes - talk to your doctor or qualified exercise professional before continuing with any physical activity program.

You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.

The authors, the PAR-Q+ Collaboration, partner organizations, and their agents assume no liability for persons who undertake physical activity and/or make use of the PAR-Q+ or ePARmed-X+. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.

PARTICIPANT DECLARATION
- All persons who have completed the PAR-Q+ please read and sign the declaration below.

If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that the community/fitness center may retain a copy of this form for records. In these instances, it will maintain the confidentiality of the same, complying with applicable law.

NAME ___________________________________________ DATE ______________________

SIGNATURE ___________________________________________ WITNESS ______________________

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER ___________________________________________

For more information, please contact
www.eparmed.com
Email: eparmed@gmail.com

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

Citation for PAR-Q+
Warburton DC, Janiuk V, Bender S, and Geddes N. on behalf of the PAR-Q+ Collaboration. The Physical Activity Readiness Questionnaire for Everyone (PAR-Q) and the Personal Physical Activity Readiness Medical Examination (P-ParQ). Health & Fitness Journal of Canada 422:3-23, 2011.

Key References
1. Jannik V, Warburton DC, & Geddes N. on behalf of the PAR-Q+ Collaboration. The Physical Activity Readiness Questionnaire for Everyone (PAR-Q) and the Personal Physical Activity Readiness Medical Examination (P-ParQ). Health & Fitness Journal of Canada 422:3-23, 2011.

2. Warburton DC, Jannik V, & Geddes N. on behalf of the PAR-Q+ Collaboration. The Physical Activity Readiness Medical Examination (P-ParQ). Health & Fitness Journal of Canada 422:3-23, 2011.


Appendix E  

Sleep Condition Indicator

Sleep Condition Indicator


Participant ID: ____________

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
</tr>
<tr>
<td><em>Thinking about a typical night in the last month...</em></td>
<td></td>
</tr>
<tr>
<td>1. ... how long does it take you to fall asleep?</td>
<td></td>
</tr>
<tr>
<td>0 - 15 min</td>
<td></td>
</tr>
<tr>
<td>2. ... if you then wake up during the night ... how long are you awake for in total?</td>
<td></td>
</tr>
<tr>
<td>0 - 15 min</td>
<td></td>
</tr>
<tr>
<td>(add all the wakenings up)</td>
<td></td>
</tr>
<tr>
<td>3. ... how many nights a week do you have a problem with your sleep?</td>
<td></td>
</tr>
<tr>
<td>0 - 1</td>
<td></td>
</tr>
<tr>
<td>4. ... how would you rate your sleep quality?</td>
<td>Very good</td>
</tr>
<tr>
<td><em>Thinking about the past month, to what extent has poor sleep...</em></td>
<td></td>
</tr>
<tr>
<td>5. ... affected your mood, energy, or relationships?</td>
<td>Not at all</td>
</tr>
<tr>
<td>6. ... affected your concentration, productivity, or ability to stay awake</td>
<td>Not at all</td>
</tr>
<tr>
<td>7. ... troubled you in general</td>
<td>Not at all</td>
</tr>
<tr>
<td>Finally ...</td>
<td></td>
</tr>
<tr>
<td>8. ... how long have you had a problem with your sleep?</td>
<td>I don't have a problem / &lt; 1 mo</td>
</tr>
</tbody>
</table>

Add the item scores to get your total score (between 0 and 32).
A higher score means better sleep.
Item scores in the grey area represent threshold criteria for Insomnia Disorder.
### Appendix F  Fear Avoidance Behavior after Traumatic Brain Injury Questionnaire

**FAB-TBI version 1.1 (January 10, 2018)**

**Participant ID:** ____________  
**Age:** ____________

**Instruction:** Please rate how much you agree with each of these statements as they apply to you over the past month.

<table>
<thead>
<tr>
<th></th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>I have put parts of my life on hold.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>I have avoided my usual activities.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>I cannot do activities which (might) make my symptoms worse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>My work might harm my brain.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>I should not do my normal work with my present symptoms.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>My head pain is telling me that I have something dangerously wrong.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>I worry that when I have to think or concentrate too hard that I will bring on a headache.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>My headaches put my head and brain at risk for the rest of my life.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>I purposely avoid doing activities that might elicit a headache.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>I'm afraid that I might make my headache pain worse by concentrating too much or being too mentally active.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>I wouldn't have this much pain if there weren't something potentially dangerous going on in my head.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>I avoid external reminders of a stressful experience (for example, people, places, conversations, activities, objects, or situations).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>I stop what I am doing when my symptoms start to get worse.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>If I know that something will make my symptoms worse I don’t do it anymore.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Because of my symptoms most days I spend more time resting than doing activities.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Most days my symptoms keep me from doing much at all.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Appendix G  
Symptom Scale

Participant ID:_________________  Age:_________________

**Concussion Grading Scale**

The Post Concussion Symptom Scale is essentially a “state” measure of perceived symptoms associated with concussion. That is, the athlete is asked to report his or her “current” experience of symptoms. This allows tracing of symptoms over very short intervals, such as consecutive days or every few days.

**Directions:** After reading each symptom, please circle the number that best describes the way the athlete has been feeling today. A rating of 0 means they have not experienced this symptom today. A rating of 6 means they have experienced severe problems with this symptom today.

**Date tested:**______________  **Date(s) of Last Known Concussion(s):**____________________

<table>
<thead>
<tr>
<th>SYMPTOMS</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Nausea</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Balance Problems</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Trouble Falling Asleep</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Sleeping More Than Usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Sleeping Less Than Usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Sensitivity to Light</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Sensitivity to Noise</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Irritability</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Sadness</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Nervousness</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Feeling More Emotional</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Numbness or Tingling</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Feeling Slowed Down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Feeling Mentally “Foggy”</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Difficulty Concentrating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Difficulty Remembering</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Visual Problems (double vision, blurring, etc.)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

**TOTAL SYMPTOM SCORE:**

**GRAND TOTAL OF ALL SYMPTOMS:**
Appendix H  Vestibular/Ocular Motor Screening

**VOMS SCORING SHEET**

Symptoms on a 0 - 10 (severe) scale

Modified from Mucha A, Collins MW, Elbin RI, Furman JM, Troutman-Enseki C, DeWolf RM, Marchetti G, Kontos AP.

<table>
<thead>
<tr>
<th>Vestibular/Ocular Motor Test</th>
<th>N/T</th>
<th>Headache</th>
<th>Dizziness</th>
<th>Nausea</th>
<th>Fogginess</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Symptoms (Pre VOMS)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Smooth Pursuit</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Saccades (horizontal)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saccades (vertical)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Convergence (NPC) #1 _____ cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#2 _____ cm</td>
<td></td>
<td></td>
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<tr>
<td>normal 5 cm or &lt; (2”)</td>
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<td></td>
<td></td>
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<tr>
<td>#3 _____ cm</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>VOR Horizontal (180 bpm)</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>VOR Vertical (180 bpm)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual Motion Sensitivity (50 bpm)</td>
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</tr>
</tbody>
</table>

*Brief Instructions: patient seated unless noted otherwise. 9-40 y/o, 1 day or > after injury*

Pursuit - one stick, 3’ away and level with patient’s nose, move stick slowly 1.5’ to the left and 1.5’ to the right

  Repeat moving stick vertically. Slow: 2 seconds to go L to R & again L to R. 2 repetitions each direction.

Saccade - start 2 sticks, 3 feet away and level with patient’s nose. Each stick 1.5’ to the left and right of nose,

  Look over & back 10x. Repeat vertically. Patient is to move eyes as fast as they can.

NPC - 1 stick, 3’ away and level with patient’s nose. Move stick slowly towards nose.

  Stop when they report seeing double or you see an eye turn/drift. Measure distance to nose.

VOR - Hold one stick, 3’ away and level with patient’s nose. Speed of head movement, 180 bpm.

  Patient turn head 20 degrees left and right, 10 times maintaining focus on target. Repeat vertically.

Visual Motion Sensitivity - Standing, patient holds stick or thumb; arms reach in front of nose.

  While maintaining fixation on stick, rotate head arms and trunk left and right 80 degrees 5x @50 bpm.
Appendix I  BORG Rating of Perceived Exertion

6  No exertion at all
7  Extremely light
8  Very light
9  Light
10
11
12
13  Somewhat hard
14
15  Hard  (heavy)
16
17  Very hard
18
19  Extremely hard
20  Maximal exertion

Instructions to the Borg-RPE-Scale®

During the work we want you to rate your perception of exertion, i.e. how heavy and strenuous the exercise feels to you and how tired you are. The perception of exertion is mainly felt as strain and fatigue in your muscles and as breathlessness or aches in the chest.

Use this scale from 6 to 20, where 6 means “No exertion at all” and 20 means “Maximal exertion.”

9 Very light. As for a healthy person taking a short walk at his or her own pace.

13 Somewhat hard. It still feels OK to continue.

15 It is hard and tiring, but continuing is not terribly difficult.

17 Very hard. It is very strenuous. You can still go on, but you really have to push yourself and you are very tired.

19 An extremely strenuous level. For most people this is the most strenuous exercise they have ever experienced.

Try to appraise your feeling of exertion and fatigue as spontaneously and as honestly as possible, without thinking about what the actual physical load is. Try not to underestimate, nor to overestimate. It is your own feeling of effort and exertion that is important, not how it compares to other people’s. Look at the scale and the expressions and then give a number. You can equally well use even as odd numbers.

Any questions?
# Buffalo Concussion Bike Test

<table>
<thead>
<tr>
<th>Time</th>
<th>Speed</th>
<th>Incline / Resistance</th>
<th>Heart Rate</th>
<th>Borg</th>
<th>Symptom changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>0m</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>1m</td>
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<td>2m</td>
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<td>3m</td>
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<td>5m</td>
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<td>6m</td>
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<td>8m</td>
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<td>9m</td>
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<td>11m</td>
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<tr>
<td>16m</td>
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<tr>
<td>17m</td>
<td></td>
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</tr>
<tr>
<td>18m</td>
<td></td>
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</tr>
</tbody>
</table>

- Complete (90% HRmax w/out sx exacerbation)
- Not complete due to: □ Symptom exacerbation □ Deconditioning □ Other