2017

Physiological, Psychological, and Behavioural Sequelae of Concussion in a Classical Conditioning Paradigm

Sabrina Freund
University of Windsor

Physiological, Psychological, and Behavioural Sequelae of Concussion in a Classical Conditioning Paradigm

By

Sabrina Freund

A Dissertation
Submitted to the Faculty of Graduate Studies
through the Department of **Psychology**
in Partial Fulfillment of the Requirements for
the Degree of **Doctor of Philosophy**
at the University of Windsor

Windsor, Ontario, Canada

2017

Physiological, Psychological, and Behavioural Sequelae of Concussion in a Classical Conditioning Paradigm

by

Sabrina Freund

APPROVED BY:

_____

L. Mainwaring, External Examiner
University of Toronto

_____

K. Milne
Department of Kinesiology

_____

L. Buchanan
Department of Psychology

_____

L. Erdodi
Department of Psychology

_____

C. Abeare, Advisor
Department of Psychology

November 13, 2017

DECLARATION OF ORIGINALITY

I hereby certify that I am the sole author of this thesis and that no part of this thesis has been published or submitted for publication.

I certify that, to the best of my knowledge, my thesis does not infringe upon anyone's copyright nor violate any proprietary rights and that any ideas, techniques, quotations, or any other material from the work of other people included in my thesis, published or otherwise, are fully acknowledged in accordance with the standard referencing practices. Furthermore, to the extent that I have included copyrighted material that surpasses the bounds of fair dealing within the meaning of the Canada Copyright Act, I certify that I have obtained a written permission from the copyright owner(s) to include such material(s) in my thesis and have included copies of such copyright clearances to my appendix.

I declare that this is a true copy of my thesis, including any final revisions, as approved by my thesis committee and the Graduate Studies office, and that this thesis has not been submitted for a higher degree to any other University or Institution.

ABSTRACT

Mild traumatic brain injury (mTBI) has been identified as a major public health concern that places individuals at risk for psychological distress, including anxiety (Mooney & Speed, 2001). Research employing rodent models of mTBI have suggested that changes in aversive conditioning underlie this increased risk, and separate models examining psychological and behavioural factors have identified dysfunctional illness representations and coping as potential mechanisms. The present study included 30 participants (15 concussed athletes, 15 non-concussed non-athletes) that were matched on age, education, and both past and current anxiety and depression. All participants completed measures of coping and emotional symptoms (depression, anxiety, and stress), provided two salivary cortisol samples (at the beginning and end of the experiment), and completed two classical conditioning tasks (pleasant and aversive) while heart rate and skin conductance responses were recorded. Background information, including history of head injuries, was collected for all participants. Concussed athletes completed an additional measure of illness representations. The results indicate that athletes demonstrated faster reaction times to the conditioned stimulus during the acquisition phase of the aversive task, and higher expectancy ratings to the conditioned stimulus during the generalization phase of both the pleasant and aversive task. Further exploratory analyses also revealed a pattern in which athletes had higher expectancy ratings to the conditioned stimulus in the first trial of both the generalization and extinction phases of both tasks. There were no differences in any of the other measures of associative learning, or in cortisol-related stress responses. In terms of coping, approach

coping strategies were found to partially mediate the relationship between illness beliefs of personal control and post-concussive symptoms. In addition, correlations between cyclical timeline beliefs and poor outcome were identified. Implications and directions for future research are discussed.

DEDICATION

To my mom and dad, for their endless love and support.

ACKNOWLEDGEMENTS

First and foremost, I would like to thank my family and my partner. To my parents, your faith in my abilities has never wavered, and your support throughout this journey – physically, emotionally, financially - has meant everything to me. To Kat, you probably understand the anxiety I felt during this process better than anyone else. Our sister-to-sister conversations always left me feeling understood and hopeful! To Chris, thanks for always making me laugh and helping me to realize the important things in life. I couldn't ask for a better little brother! To my partner Mike, there are not enough words. Your understanding and support have far exceeded my expectations throughout this process. You've been there to celebrate every success, to calm every nerve, and to wipe away every tear. I love you.

This dissertation would not have been possible without the support and guidance of my research advisor, Dr. Christopher Abeare. Chris, I joined your research lab 9 years ago as an undergraduate. You've helped me grow as a researcher, a clinician, and a person ever since. Your belief in my ability to complete a doctorate in neuropsychology more often than not exceeded my own, and your advice and kind words never failed to reduce my anxiety or to motivate me. I couldn't have done this without you!

There have been many people who have been involved in this research and without them I would not have been able to complete my dissertation. I would like to thank Dr. Lori Buchanan, Dr. Laszlo Erdodi, and Dr. Kevin Milne for serving on my dissertation committee and offering guidance and insight at various points. Thank you as well to Dr. Lynda Mainwaring for providing your expertise as my external reader. Thank you to my research assistant Ben Guins for taking over data collection when I could no longer be physically present in Windsor. I would also like to thank the wonderful administrative staff within the Psychology department.

Finally, I would like to thank all of my friends and colleagues. To my University of Windsor Psychology friends, we've made it! These years have been hard, but we've woven in periods of laughter and countless good memories, and formed friendships that will last a lifetime. Thank you for all of your support along the way. To my friends

outside of school, thank you for understanding when I was too busy or stressed to see you, but always being there when I needed you. Your support has meant more than you know.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1
INTRODUCTION

Although the significance of moderate and severe brain injuries has long been recognized, the impact of milder brain injuries, including concussions, has only recently been appreciated. Interest in mild traumatic brain injury (mild TBI; mTBI) has recently been piqued by news of late-life dysfunction and autopsies of a number of professional athletes engaged in high-contact sports, particularly football. Whereas the vast majority of individuals recover fully from concussion, there is a small but significant group that continues to exhibit cognitive, somatic, and affective symptoms beyond 3-months post-injury (Kraus & Chu, 2005). Such prolonged symptoms are referred to as post-concussion syndrome.

Further, evidence suggests that a mild brain injury places individuals at risk for the acquisition of a variety of anxiety disorders, including posttraumatic stress disorder (PTSD), generalized anxiety, and social phobia (Mooney & Speed, 2001). Of particular interest in the present study were symptoms of anxiety occurring in the acute phase of concussion, presenting as either part of the clinical picture of post-concussion syndrome or the acquisition of specific anxiety disorders.

One major line of research has focused on the neuroanatomical substrates of aversive classical (Pavlovian) conditioning as a critical component in the acquisition and maintenance of anxiety disorders. Normal aversive conditioning relies on a vast network of brain structures collectively referred to as the "fear circuit," including the amygdala, hippocampus, insula, anterior cingulate cortex, and other regions of the prefrontal cortex (Sehlmeyer et al., 2009). Animal models of mild TBI and limited neuroimaging studies in humans suggest that, even in the absence of gross pathology, these areas exhibit

microscopic structural changes and dysfunction following injury (Giza & Hovda, 2014). Further, rodent models of concussion that examined changes in aversive conditioning and anxiety behaviours revealed increased aversive conditioning and generalization, as well as increases in a variety of anxiety-like behaviours (e.g. Reger et al., 2012; Almeida-Suhett et al., 2014). As of yet, these connections have not been established in human mild TBI samples.

A separate line of research has focused on psychological factors impacting recovery following mTBI. Recently, a limited number of studies have used the Common Sense Model (CSM; Leventhal, Leventhal, & Contrada, 1998) as a paradigm for understanding the impact of illness representations and coping strategies on outcome in mild TBI samples specifically (Snell, Siegert, Hay-Smith, & Surgenor, 2011; Snell, Hay-Smith, Surgenor, & Siegert, 2013; van Wilgen, Kaptein, & Brink, 2010). These studies have typically focused on concussion symptoms as outcome variables, with less emphasis on affective symptoms specifically. Further, these studies have focused solely on the independent effects of illness representations and coping strategies, and have neglected to investigate the mediational relationship of illness representations, coping, and outcome proposed by the CSM.

A review of the literature identifies a gap in our understanding of the risk for increased anxiety and diagnosed anxiety disorders following mild traumatic brain injury. It also reveals that previous work has examined either physiological or psychological/behavioural risk factors in isolation, even though the need to consider both of these factors has been identified (Silverberg & Iverson, 2011). The present study

attempts to extend and integrate previous literature on rodent models of mild TBI and the CSM to fill this knowledge gap.

CHAPTER 2

LITERATURE REVIEW

Concussion

Definition, Prevalence, and Cause

Traumatic Brain Injury (TBI) is a major public health concern. In the United States alone, it is estimated that 1.8 million to 3.8 million brain injuries occur annually (Faul, Xu, Wald, & Coronado, 2010; Langlois, Rutland-Brown, & Wald, 2006), with 75% of those injuries classified as mild (mTBI; Gerberding & Binder, 2003). This classification of severity is based largely on the fact that these injuries involve only a brief alteration of mental status, in comparison to the prolonged periods of unconsciousness and posttraumatic amnesia associated with moderate and severe brain injuries (Centers for Disease Control and Prevention, 2004). Despite the classification of these injuries as mild, the economic impact is substantial, with mTBI accounting for approximately 44% of the $56 billion annual cost of TBI in the United States alone (Thurman, 2001). In 2010, the economic cost of TBI in the United States was estimated to be even higher at $76.5 billion (Centers for Disease Control and Prevention, 2016).

Diagnosis of concussion is typically made based on a combination of subjective report of symptoms and signs, neuroimaging findings, balance testing, and cognitive testing. The range of symptoms include: somatic symptoms (e.g. headache); cognitive symptoms (e.g., feeling like in a fog); and/or emotional symptoms (e.g., lability). There may also be physical signs (e.g., loss of consciousness, amnesia), behavioural changes

(e.g., irritability), cognitive impairment (e.g., slowed reaction times), and sleep disturbance (e.g., insomnia; McCrory et al., 2013). Within sports, suspected concussions are often examined on the side-line using brief neuropsychological measures such as the Sideline Concussion Assessment Tool (SCAT3) or Standardized Assessment of Concussion (SAC; McCrory et al., 2013). Concussion is associated with negative findings on conventional diagnostic imaging. Thus, CT and MRI scans are typically employed only to test for the presence of hematomas and to rule out complications from more severe head injuries (Eierud et al., 2014). As a result of the lack of diagnostic markers on conventional neuroimaging tests and an emphasis on subjective symptoms, concussions are often undiagnosed or misdiagnosed. This problem may be compounded in athletes motivated to stay in play, who either under-report or do not report their symptoms at all (Rabinowitz, Li, & Levin, 2013), or in cases of litigation where individuals can be motivated to over-report symptoms (Belanger, Curtiss, Demery, Lebowitz, & Vanderploeg, 2005).

The terms mTBI and concussion are used as labels for mild forms of head injury, although their use does not have general agreement. These terms are often used interchangeably, but recently, some researchers have argued for distinction between the terms "mTBI" and "concussion" (McCrory et al., 2013) based on arguments that the general public does not see the terms as synonymous. In the debate regarding mTBI and concussion terminology, Ehmed and Sullivan (2015) examined 122 contact-sport players and their reactions to sport-related vignettes that varied only in the diagnostic label applied to each vignette (i.e., concussion, mTBI, or no diagnosis). Participants rated their injury perceptions, including perceived undesirability, chronicity, and consequences of

the injury, as well as their expectations of poor outcome. The results showed that there were no differences in players' perceptions or symptom expectations based on the diagnostic label provided. For the time being, most experts agree that concussion represents a form of mTBI, with no more than a transient disruption of function (Rabinowitz et al., 2014). Definitions of concussion/mTBI vary slightly based on the specific group providing the definition. For example, the Centers for Disease Control (CDC) and Prevention's Mild Traumatic Brain Injury Working Group define a concussion as "the occurrence of injury to the head arising from blunt trauma or acceleration or deceleration forces with one or more of the following conditions attributable to the head injury:

- any period of observed or self-reported
    - transient confusion, disorientation, or impaired consciousness,
    - dysfunction of memory around the time of injury, or
    - loss of consciousness lasting less than 30 minutes;
- observed signs or other neurological or neuropsychological dysfunction, such as
    - seizures acutely following the injury to the head,
    - irritability, lethargy, or vomiting following head injury, or
    - headache, dizziness, irritability, fatigue or poor concentration."

The Mild Brain Injury Special Interest Group of the ACRM (American Congress of Rehabilitation Medicine) provides a slightly different definition: "a patient with a mild TBI is a person who has had a traumatically induced physiological disruption of brain function, as manifested by at least one of the following:

- any period of loss of consciousness

- any loss of memory for events immediately before or after the accident,
- any alteration in mental state at the time of the accident (e.g., feeling dazed, disoriented, or confused), or
- focal neurological deficits that may or may not be transient."

The 5th International Conference on Concussion in Sport (McCrory et al., 2017) led to the release of a consensus statement that defined a sport related concussion (SRC) specifically as a "traumatic brain injury induced by biomechanical forces. Several common features that may be utilised in clinically defining the nature of a concussive head injury include:

- SRC may be caused either by a direct blow to the head, face, neck or elsewhere on the body with an impulsive force transmitted to the head.
- 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 a number of minutes to hours.
- 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.
- SRC results in a range of clinical signs and symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive features typically follows a sequential course. However, in some cases symptoms may be prolonged.

The clinical signs and symptoms cannot be explained by drug, alcohol, or medication use, other injuries (such as cervical injuries, peripheral vestibular dysfunction, etc.) or other comorbidities (e.g., psychological factors or coexisting medical conditions)."

What is clear from the above definitions is that a concussion is generally conceptualized as a transient condition with some change in mental state resulting from trauma to the head, either as a direct force to the head or as the result of acceleration-deceleration forces. Other aspects of the definitions vary, with differential importance placed on neurological signs and symptoms. According to Bigler (2008), definitions of concussion have four dominant features common to all: 1) brief alteration in consciousness or neurological function with at least acute changes in mentation and speed of processing, 2) physical symptoms of fatigue, headache, dizziness, and/or vertigo, 3) impairments in short-term memory, attention, and concentration, and 4) increased likelihood for changes in mood and affective functioning. A number of groups (e.g., Mild Brain Injury Special Interest Group) delineate at which point a more severe diagnosis of brain injury should be given; this includes a period of loss of consciousness longer than 30 minutes, posttraumatic amnesia (PTA) lasting longer than 24 hours, or a Glasgow Coma Scale (GCS) assessed at less than 13. The GCS assesses motor, verbal, and eye responses, and ranges from 3-15 with higher scores indicating higher levels of functioning.

There are a wide range of situations and events that may lead to a head injury. Common causes of mTBI include motor vehicle accidents (MVAs), falls (especially in the very young and in older adults), assault, or struck by/against events (Faul et al., 2010). Mild TBI injuries are also frequently sustained in military combat; 5% of army

infantry soldiers reported injuries with loss of consciousness and 10% reported injuries with altered mental status during a year-long deployment to Iraq (Hoge et al., 2008). Recent work suggests even higher rates in this population, with up to 23% of army personnel screening positive for clinician-confirmed TBI history (Terrio et al., 2009.) Finally, participation in sports can lead to brain injuries; one estimate suggested that approximately 300,000 sports-related concussions occur annually in the US (Thurman, Branche, & Sniezek, 1998). It should be noted that this estimate included only concussions that involved a loss of consciousness. Given that as many as half of sports-related concussions go unreported (McCrea, Hammeke, Olsen, Leo, & Guskiewicz, 2004), and that only between 8% and 19.2% of these reported injuries are thought to involve a loss of consciousness (Langlois, Rutland-Brown, & Wald, 2006), this number is likely an underestimate. Langlois, Rutland-Brown, and Wald (2006) estimate that anywhere between 1.6 and 3.8 million total sports-related TBIs occur each year. High contact sports are most likely to cause concussions, with 4-20% annual incidence of mTBI in football (Mendez, Hurley, Lassonde, Zhang, & Taber, 2005). Among high school, college, and amateur athletes, ice hockey and rugby have the highest incidence of concussion. At the recreational level, female taekwondo participants and male boxers have the highest frequency of concussion (Mendez et al., 2005).

Biomechanics of Concussion

Biomechanics is defined as the study of biological systems, such as the brain, in response to physical forces. In mTBI, mechanical forces can damage the brain directly through the immediate consequence of deformation and strain, as well as indirectly

through delayed damage caused by the initiation of physiological processes leading to cell dysfunction or death (Giza & Hovda, 2014).

Two important types of forces may play a role in the biomechanics of a concussion: linear acceleration and rotational/angular acceleration. Early estimates of injury tolerance levels (the likelihood that an individual will sustain a concussion at an impact of a given magnitude) proposed that impacts of 90 g linear acceleration sustained for 9 milliseconds or longer were sufficient to produce mTBI (Ono & Kanno, 1996). Further research presented a more complicated picture. For example, some studies have shown that linear acceleration as low as 60 g is sufficient to produce concussion (Guskiewicz et al., 2007b), whereas others have shown that athletes can sustain impacts greater than 90 g without any neurological dysfunction (McCaffrey, Mihalik, Crowell, Shields, & Guskewicz, 2007). Thus, the relationship between impact force and injury appears to not be direct, but rather moderated by other factors. In terms of rotational acceleration, this is the type of acceleration that is thought to contribute most to concussion (King, 2003). These rotational forces produce the shearing of axons and deeper lesions; fronto-subcortical areas have proven particularly vulnerable to this type of acceleration (Williamson, Heilman, Porges, Lamb, & Porges, 2013).

A combination of variables appears to better predict who will sustain a concussion than any single variable in isolation. For example, Greenwald, Gwin, Chu, and Crisco (2008) found that the best predictor of concussion was an algorithmic combination of linear acceleration, rotational acceleration, Head Injury Criterion (HIC; a formula that estimates the likelihood of head injury from impact by taking into account both acceleration and time), and impact location. Similar results were obtained by Broglio and

colleagues (2010) who found that concussion was most likely to occur when linear acceleration exceeded 96.1 gs, rotational acceleration exceeded 5,582 rad/sec^2, and impact location was r the front, side, or top of the helmet.

Other studies have modelled the impact of acceleration and deceleration forces. For example, Viano and associates (2005) simulated movement within the cranium during concussion using finite element analysis and constructing a detailed anatomic model of the brain and head accelerations based on game impacts from National Football League (NFL) videotapes of injured players. These models indicated that the largest strains occurred in the fornix, midbrain, and corpus callosum. In particular, the hippocampus, caudate, amygdala, anterior commissure, and midbrain showed 4-5mm displacements. As will be discussed in subsequent sections, structural changes and the dysfunction of these medial structures may play a role in the acquisition of anxiety disorders due to their role in classical conditioning, a type of associative learning that has been implicated in both the acquisition and maintenance of anxiety.

Neuropathology

There appears to be an absence of any clear morphological or functional abnormalities in the brains of individuals sustaining a mild TBI (Bigler & Maxwell, 2012). Specifically, conventional imaging techniques such as Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) are either negative for any abnormal findings, or show only minimal levels of damage (Bazarian et al., 2013). In the absence of overt macroscopic brain pathology, however, mTBI is typically associated with microscopic brain pathology, specifically widespread axonal injury. Known as diffuse axonal injury (DAI), this type of damage can be detected via newer forms of

neuroimaging techniques such as Diffusion Tensor Imaging (DTI; Bazarian et al., 2013). Given that axons are particularly vulnerable to mechanical injury due to their viscoelastic properties, diffuse axonal injury (DAI) is common after mTBI. For example, Browne, Chen, Meaney, and Smith's (2011) porcine models of mTBI revealed multifocal axonal pathology. Similarly, as discussed in detail later, DTI has been used to examine neuropathology in humans with concussion, and has revealed evidence for widespread axonal injury (e.g., Zhang, Heier, Zimmerman, Jordan, & Ulug, 2006).In addition to the diffuse axonal injury that is incurred by some following concussion, research has revealed a cascade of neurochemical changes that begin immediately following the impact or force causing the head injury.

Neurochemical Changes

Giza and Hovda (2014) provide a comprehensive review of the current understanding of the neuropathology of concussion using rodent models. Based on their research, they define concussion as a "neurometabolic cascade of events" that includes: ionic flux and glutamate release, an energy crisis, cytoskeletal damage, axonal dysfunction, altered neurotransmission, inflammation, and cell death. This metabolic cascade is initiated by biomechanical forces that lead to the opening of ion channels via the disruption of neuronal membranes and axonal stretching. The opening of these channels causes uncontrolled ionic flux with an efflux of potassium and an influx of sodium and calcium into the cell. Further depolarization is caused by a hyperacute indiscriminate release of the excitatory neurotransmitters glutamate. In an effort to restore ionic homeostasis, sodium potassium pumps relying on adenosine triphosphate (ATP) must work harder than usual. Hyperglycolysis, an energy-demanding process, occurs as

the cell converts increased amounts of adenosine diphosphate (ADP) into ATP. The combination of decreased cerebral blood flow, diminished glucose availability, and an increased need for glucose leads to an energy crisis in the brain. After this initial period of hyperglycolysis, glucose metabolism becomes impaired for a period of 7-10 days. The cytoskeletal damage caused by the biomechanical forces of concussion affects the dendritic arbors and axons of both neurons and glial cells, which provide support and protection for neurons. Concussion has also been linked to changes in inflammatory markers, shown by upregulation of cytokine and inflammatory genes (Li, Lee, Cai, Sutton, & Hovda, 2004; Patterson & Holahan, 2012).

Research employing non-human animal models of mTBI suggests that within 10 days of injury, chemical and metabolic levels return to normal (Hovda, Yoshino, Kawamata, Katayama, & Becker, 1991; Yoshino, Hovda, Kawamata, & Becker, 1991). This is consistent with neuropsychological functioning in humans demonstrating a 10-day recovery curve (Belanger & Vanderploeg, 2005). The pathophysiological changes of concussion map onto a number of clinical signs and symptoms. For example, the brain's increased need for energy within the acute recovery period is consistent with an increased vulnerability to a second injury during this time for both humans and animals (Guzkiewicz et al., 2003; Bigler, 2008). Further, symptom exacerbation with physical exertion is commonly reported during this time, providing additional evidence that the brain experiences an increased need for energy during this acute phase (Leddy et al., 2010). Giza and Hovda (2014) proposed a number of additional connections between the neurobiology of concussion and early clinical symptoms: ionic flux and migraine, photophobia, and phonophobia; axonal dysfunction and impaired cognition, slowed

processing, and slowed reaction times; impaired neurotransmission and impaired cognition, slowed processing, and slowed reaction time; and protease activation, altered cytoskeletal proteins, and cell death, and chronic atrophy and development of persistent impairments. In addition to specific symptoms, neurometabolic changes of decreased glutamate in the acute phase of concussion correlate with self-reported symptom severity (Henry, Tremblay, Boulanger, Ellemberg, & Lassonde, 2010).

Many of the above findings were based on non-human animal models of brain injury. Of course, it is also important to validate these mTBI models in human populations. On this note, Bergsneider and colleagues (2001) found reduced glucose metabolism for approximately one month following mild to severe TBI in a patient sample. Zetterberg et al. (2006) examined markers of neuronal and astroglial injury in the cerebrospinal fluid (CSF) of amateur boxers and found that indicators of neuronal injury by-products were significantly related to the number of hits taken during a bout. These acute pathological changes were found despite the fact that the hits were subconcussive in nature. In a group of professional boxers, Zhang, Heier, Zimmerman, Jordan, and Ulug (2006) found subtle white matter abnormalities using DTI techniques. These results were replicated by Chappell and colleagues (2006) in a group of 81 professional boxers. Finally, Cohen and associates (2007) found subtle brain volume loss in a 20 patient sample of mild TBI. These studies suggest that the glucose hypometabolism, axonal damage, and cell death seen in animal models are consistent with the neuropathology of concussion in humans.

Structural Changes

Researchers examining rodent models of brain injury have employed a number of different injury mechanism procedures including: lateral fluid percussion (LFP) injury (Lifshitz, Witgen, & Grady, 2007; Reger et al., 2012), blast overpressure (Genovese et al., 2013; Elder et al., 2012), controlled cortical impact (CCI; Almeida-Suhett et al., 2014), and weight-drop procedures (Meyer et al., 2012). These procedures differ in a number of ways, including severity and level of invasiveness. Despite these differences, these experimental procedures in rodents produce similar pathological features to those characteristic of brain injury in humans, specifically neuronal loss, gliosis, and metabolic and ionic perturbations (Lifshitz et al., 2007).

These studies overall have found a lack of gross pathology, consistent with the mTBI presentation seen in human populations, but have identified axonal degeneration and loss of neurons as a consequence of mild TBI procedures in rats. For instance, Heldt and colleagues (2014) observed scattered axonal degeneration in brain sections of mice 3-8 weeks after blast-induced trauma in spite of a lack of gross cerebral pathology. This pattern of neuronal loss is consistent with the diffuse axonal injury characteristic of mild TBI in humans. In addition, despite the lack of gross pathology following a single mild TBI, some functional impairment over multiple injuries suggests that there may be some chronic long-term structural changes (DeFord et al., 2002).

In addition to diffuse microstructural changes, some research suggests changes in structural volume in specific regions, including the amygdala and hippocampus. The amygdala and hippocampus are bilateral structures located deep within the temporal lobes that, as a result of their location in the brain, may be particularly vulnerable to the rotational acceleration forces and the neurometabolic cascade associated with concussion.

The amygdala is an almond-shaped structure comprising 13 nuclei, which can be divided into three major groups: deep or basolateral group, superficial or cortical-like group, and the centromedial group. It plays an important role in emotional processing, particularly the processing of fear. The hippocampus is a seahorse-shaped structure found adjacent to the amygdalae that plays an important role in emotional responding and human memory. More detailed information regarding the function of these structures is discussed in subsequent sections.

Meyer et al. (2012) discovered neuronal cell loss in the dorsal hippocampus and increased cell numbers in subregions of the amygdala. Similarly, Lifshitz and colleagues (2007) found significant neuronal loss in the hippocampus, but not in the amygdala. In spite of the literature indicating no reduction in the overall number of neurons within the amygdala, studies focused on Thy1 excitatory projection neurons specifically have found evidence of decreased neurons. In two separate studies, mice receiving overpressure air blasts of 50-60 psi showed decreased numbers of Thy1 enriched neurons in the basolateral amygdala two months after blast, with reductions by 25% (Heldt et al., 2014) and 20% (Reiner et al., 2015), respectively. The functional implications of these disturbances on anxiety and fear processes will be described below.

There have been efforts to investigate structural changes in humans using a wide range of neuroimaging techniques, including Positron Emission Tomography (PET), Single-Photon Emission Computed Tomography (SPECT), Magnetoencephalography (MEG), Electroencephalography (EEG), Magnetic Resonance Imaging (MRI), and subtypes of MRI including DTI, functional MRI (fMRI), and Magnetic Resonance Spectroscopy (MRS). A review of neuroimaging results by Belanger, Vanderploeg,

Curtiss, and Warden (2007) indicated that there are at least some abnormalities associated with mild TBI across imaging modalities. Their qualitative review of these studies suggested that many of the results indicate structural changes relating to mild TBI.

Possibly the most sensitive structural imaging technique to the effects of mTBI is DTI, which allows for the examination of the structural integrity of white matter tracts by calculating the amount of directional restriction of water movement in the brain. When water is unrestricted, it diffuses equally in all directions (isotropic), but when it is restricted, it will not diffuse equally in all directions (anisotropic). The type of diffusion is dependent largely on the type of tissue present; for example, in CSF the water is largely unrestricted, but along axons and myelin sheaths the water is generally restricted to a movement that is parallel to white matter tracts, due to the fact that white matter is made of lipids and lipids are hydrophobic (Shenton et al., 2012). There are a number of DTI measures, with functional anisotropy (FA) values most commonly used as a sensitive, but non-specific, marker of neuropathology and microstructural change (Alexander, Lee, Lazar, & Field, 2007). This value provides a marker of the shape of the diffusion; unrestricted diffusion typically creates a spherical shape while restricted diffusion created an elongated ellipsoid.

Mild TBI research employing DTI measures have found mixed evidence for FA values in the acute phase of concussion, with some finding decreased FA values (e.g., Matsushita et al., 2011) and others findings increased values (e.g., Bazarian et al., 2007). However, when examining DTI anisotropy values following mTBI across studies, there appears to be a pattern that is temporal in nature. The meta-analysis by Eierud et al. (2014) suggested that acute mTBI tends to be associated with elevated anisotropy values

and chronic mTBI tended to be correlated with depressed anisotropy levels. Both are suggestive of white matter changes, with elevated anisotropy levels thought to reflect axonal swelling processes in the acute phase, and reduced anisotropy levels related to damage of myelin or axon membranes, reduced axonal packing density, and/or reduced axonal coherence (Shenton et al., 2012).

Functional Changes

In addition to the structural changes noted above, the mild TBI literature suggests that there are abnormalities in functioning, even in areas thought to be structurally intact. Recent studies employing rodent models have examined the effects of mTBI on the function of various brain structures, particularly mesial temporal lobe structures including the amygdala (Meyer et al., 2012; Elder et al., 2012; Lifshitz et al., 2007; Reger et al., 2012) and hippocampus (Meyer et al., 2012; Lifshitz et al., 2007; Reger et al., 2012). There is evidence of amygdalar dysfunction after brain injury in rodents across a number of studies (Hovda et al., 1991; Meyer, Davies, Barr, Manzerra, & Forster, 2012). For example, Ameida-Suhett and colleagues (2014) used a blast-induced mTBI procedure in rodents and found subsequent bilateral amygdalar hyperactivity. There is also evidence of prolonged hippocampal dysfunction following mTBI in rodents (Fendt & Fanselow, 1999), including changes in inhibitory neurotransmission (Reger et al., 2012).

A number of studies have also found alterations in protein synthesis and neurotransmission in the amygdala. Specifically, with regards to protein synthesis, there is indication of an elevation in the protein stathmin 1 in the amygdala, which is crucial for the regulation of innate and learned fear (Elder et al., 2012). Research examining dysfunctional neurotransmission using rodent models has generally found increased

excitatory receptors and processes in the context of decreased inhibitory receptors and processes, with a sum excitatory effect, particularly within the basolateral amygdala (BLA). For example, changes in inhibitory neurotransmission were evidenced by decreased levels of GAD67, a biosynthetic enzyme for gamma-aminobutyric acid (GABA), in the amygdala (Reger et al., 2012). Further, these authors found a significant upregulation of excitatory N-methyl-D-aspartate (NMDA) NR1 receptors in the BLA, a trend for increased NR2A and B NMDA receptors, and a trend toward decreased GABA-related inhibition in the BLA and hippocampus. Similarly, Almeida-Suhett and colleagues (2014) found significant loss of GABAergic interneurons and significant reductions in the frequency and amplitude of spontaneous and miniature $GABA_A$-receptor mediated inhibitory postsynaptic currents (IPSCs), indicating a significant reduction of inhibition in the BLA. This was associated with reduced surface expression of α1, β2, γ2 $GABA_A$ receptor subunits. Finally, there were significant increases in the surface expression and current mediated by α7-nAChR, indicating increased excitability of principal neurons within the BLA.

There have been investigations of functional changes in humans using a wide range of neuroimaging techniques. A review of these neuroimaging results by Belanger, Vanderploeg, Curtiss, & Warden (2007) indicated that there are at least some functional abnormalities associated with mild TBI in areas found to be structurally intact.

Simmons and Matthews (2012) conducted a meta-analysis of fMRI studies for individuals with heterogenous mTBI performing a variety of tasks, mostly cognitive and motor in nature. The authors found dysregulation of function in several prefrontal, parietal, and temporal regions, specifically clusters in the superior and middle frontal

gyri, superior and inferior parietal lobules, superior temporal gyrus, and medial frontal cortex. In a different fMRI meta-analysis, areas of reduced activity included the middle frontal gyrus, right middle temporal gyrus, right precentral gyrus, and right anterior cingulate. Areas of increased activity included the right insula, right inferior parietal lobule, right cerebellar tonsil, right inferior frontal gyrus, and right supramarginal gyrus (Eierud et al., 2014). These results are generally consistent with an anterior-to-posterior pattern of activity in which there is reduced activity in anterior regions and increased activity in posterior regions. Consistent with these results are studies finding evidence of functional abnormalities in the amygdala following mild TBI. For example, following blast induced TBI, bilateral amygdalar hyperactivity has been observed in U.S. soldiers (Matthews et al., 2011).

Overall, research examining the neuropathology of concussion in rodent and human populations has found an absence of macroscopic brain pathology, in the context of microscopic brain pathology characterized by widespread axonal injury, with associated neurochemical and metabolic changes, neuronal loss and decreased volume in mesial brain structures, and both hyperactivity and hypoactivity of various brain structures. The pattern of recovery from this neuropathology and variables affecting typical outcome are discussed below.

Concussion Outcome

The majority of patients recover completely from mTBI (Iverson, 2007). Despite the minimal overt brain damage in mild TBI, current statistics indicate that about 10-15% of mTBI patients will develop persistent cognitive, behavioural, and/or emotional complaints (Kraus & Chu, 2005). Some studies have cited significantly higher rates of

poor outcome ranging from 24% to 55% by 3-months post-injury, 26% to 51% by 6-months post-injury, and 27.3% to 50% by 12-months post-injury (Snell, Siegert, Hay-Smith, & Surgenor, 2011a). These statistics are hotly debated in the literature and it is suggested that these rates may be largely inflated due to the self-report nature of measures, motivational biases, and litigation status. A large meta-analysis conducted by Binder, Rohling, and Larrabee (1997) found no lasting effects of mTBI at 3-months post-injury. This meta-analysis was updated and corroborated by Frencham, Fox, and Maybery (2005). Other researchers (Pertab, James, & Bigler, 2009; Bigler, Farrer, Pertab, James, Petrie, & Hedges, 2013) have examined the same data and concluded that the methodological flaws associated with meta-analysis hides a "lost minority," a minority of mTBI patients that suffer from persistent symptoms.

The acute outcome of concussion tends to be better in athletes, with athletes tending to show full neuropsychological recovery within 10 days, whereas concussion symptoms tend to resolve completely within three months post-injury for the general population of patients (Belanger and Vanderploeg, 2005). This difference in acute recovery may be due to a number of reasons at biomechanical, physiological, and psychological levels (Rabinowitz et al., 2014). From a biomechanical perspective, the forces involved in sports-related injuries tend to be less severe in comparison to other common injury mechanisms (i.e. motor vehicle accidents, falls) and the physical attributes of athletes, including well-developed neck musculature, help minimize rotational acceleration forces present in mTBI injuries. At the physiological level, higher pre-injury level of fitness may protect from neuronal injury and properly timed physical activity helps to promote recovery (Schneider et al., 2013). From a psychological

perspective, athletes are less likely to have comorbid psychiatric diagnoses and generally demonstrate lower stress responses, as measured by adrenocortical responses, autonomic responses, and psychological responses (e.g., Rimmele et al., 2007; Rimmele et al., 2009). A study by Verner et al. (2010) found that female athletes similarly demonstrated a lower cortisol stress response to an experimental stressor in comparison to female non-athletes. In all three of these studies baseline levels were similar across groups. A lower stress response in athlete groups may act as a protective factor in recovery. Motivation may also lead to differences in acute recovery, with the higher motivation of athletes to return to play may lead them to minimize symptoms (Rabinowitz, et al., 2014), whereas other mTBI patients may have the opposite motivation.

When examining long-term outcome, however, athletes may be at risk for chronic problems. For example, studies have shown an association between recurrent concussion and late-life cognitive dysfunction (Guskiewicz et al., 2005) and depression (Guskiewicz et al., 2007a) in retired professional football players. Furthermore, more than three decades after injury, athletes who played at university level and incurred a concussion continued to demonstrate electrophysiological abnormalities and cognitive and motor impairments when compared to matched controls with no history of concussion; specifically, they exhibited delayed and attenuated P300 brain signals, reduced movement velocity, and lower scores on tasks of episodic memory and response inhibition (De Beaumont et al., 2009).

Within the present study, emotional complaints related to symptoms of anxiety following mTBI are of interest. Anxiety following mTBI can present as part of the symptom picture of post-concussive syndrome (PCS) or as the acquisition of an anxiety

disorder subsequent to a head injury. Understanding the etiology of affective symptoms following mTBI will help in the early identification of those at risk for developing PCS and acquired anxiety disorders. Before PCS and anxiety disorders are discussed in detail, various factors that may lead to poor outcome are considered.

Factors affecting Outcome

Recovery after mTBI, including the resolution of cognitive, somatic, and affective symptoms, remains poorly understood. The majority of research suggests an interplay between psychogenic and physiogenic factors (King & Kirwilliam, 2011). One early model put forth by Lishman (1988) suggested that neurobiological factors were solely implicated in the development of symptoms, while psychological factors accounted for the maintenance of long-lasting symptoms. However, Silverberg and Iverson (2011) updated this model by reviewing research in the 20 years following Lishman's original paper, suggesting that both neurobiological and psychological factors play a role in the development and maintenance of post-concussion symptoms. Other factors that have been examined include demographic variables and factors related to injury mechanism and severity.

Demographic factors related to outcome include age, gender, and education. Research generally finds that increased age is related to poorer outcome, particularly being over the age of 40 (Binder, 1986). Female gender has widely been cited as a predictor of poor outcome, particularly PCS symptoms (Meares et al., 2008; Edna & Cappelen, 1987). A study found that females reported more PCS symptoms, but did not differ from males in respect to number of days before returning to normal functioning and number of days of work missed (Bazarian, Blyth, Mookerjee, He, & McDermott, 2010).

In terms of educational attainment, the majority of research has found that higher levels of education are associated with better outcomes (Stulemeijer, van der Werf, Borm, & Voss, 2008), although at least one study has found a correlation between higher education and increased odds of poor outcome (Snell et al., 2011a).

The majority of studies have found that injury mechanism and severity of the injury are not related to outcome. For example, in a study by Snell and colleagues (2011a) measures of injury severity, including Glasgow Coma Scale scores, duration of loss of consciousness, and posttraumatic amnesia duration did not differentiate between good and poor outcome groups. Concussion biomechanics, similarly, do not appear to play a predictive role in outcome. Guskiewicz et al. (2007b) found that there was no significant correlation between concussive impact magnitude and post-injury changes in symptoms, postural control, and cognitive functioning among collegiate athletes. Broglio, Eckner, Surma, and Kutcher (2011) replicated these findings in a sample of high school football players, finding no association between cumulative linear or rotational acceleration and post-concussive outcomes.

It has been suggested that both pre-morbid and current psychiatric and psychological variables may mediate persistent symptoms following mTBI (McCrae et al., 2009). Some of the strongest psychological predictors include prior psychiatric history (Meares et al., 2008; Carroll et al., 2004), including premorbid anxiety or depressive disorders (Meares et al., 2011), personality traits such as neuroticism (Keshavan, Channabasavanna, & Reddy, 1981), and stressful life experiences (Lidvall, Linderoth, & Norlin, 1974). Further, a history of alcohol or substance misuse is associated with poorer outcome (Lishman, 1988).

In terms of motivational factors, compensation-seeking, effort, and motivation are consistently demonstrated as the strongest predictors of outcome (Carroll et al., 2004). Meta-analysis of outcome suggested that litigation status was associated with greater cognitive sequelae that were stable or worsened over time (Belanger et al., 2005). As a result, understanding the factors that play a role in the etiology of true cases of PCS may be best achieved through the study of concussed athletes, who are generally motivated to recover quickly in an effort to return to play. Thus, in the current study, the possible development of PCS and anxiety symptoms is examined during the acute phase of concussion when individuals may be in a vulnerable neurometabolic state.

Post-Concussion Syndrome

Post-Concussion Syndrome (PCS) is defined as set of symptoms following mTBI that typically include: physical symptoms, such as headaches and dizziness; cognitive symptoms, such as problems with memory and concentration; and emotional symptoms, including irritability, anxiety, emotional lability, and depression. Cases of concussion that have not recovered within 3 months generally receive a diagnosis of PCS. Our understanding of PCS is complicated by inconsistencies in definition. The DSM-IV provided a diagnostic criteria for post-concussional disorder (PCD) in the Criteria Sets and Axes Provided for Further Study, and the ICD-10 provided a diagnostic set for PCS; however, the symptom criteria differ between these two diagnostic systems (Bigler, 2008). As a result, there are differences in prevalence rates between the two criteria sets. Specifically, prevalence rates are higher when using ICD-10 criteria (64%) than DSM-IV criteria (11%) three-months post-injury (Boake et al., 2005). PCS as a syndrome has been debated, given that the presence of post-concussion symptoms is high even in normal,

uninjured individuals. Up to 88% of healthy individuals report post-concussion syndrome-type symptoms, despite never having sustained a concussion.

There is some evidence to suggest that there is symptom overlap between PCS and anxiety disorders, including physiological symptoms such as sleep disturbance, fatigue, cognitive symptoms such as difficulty concentrating, and emotional symptoms such as irritability and feelings of anxiety. Exploratory factor analyses of the Post-Concussion Symptom Scale (PCSS; Lovell, Collins, Podell, Powell, & Maroon, 2000), a 22-item scale examining PCS, suggested a factor solution that included somatic, cognitive, sleep, and emotional factors in a group of athletes following concussion (Kontos, Elbin, Schatz, Covassin, Henry, Pardini, & Collings, 2012). Potter, Leigh, Wade, and Fleminger (2006) found a three-factor structure of cognitive, somatic, and affective factors when using the Rivermead Post Concussion Symptom Questionnaire (RPQ; King, Crawford, Wenden, Moss, & Wade, 1995), another commonly used measure for examining PCS. The presence of emotional factors in these measures underscores the similarity in symptoms between PCS and affective disorders.

In addition to significant symptom overlap, there also appears to be significant comorbidity between symptoms of emotional distress and PCS symptoms. In one sample, a measure of anxiety correlated strongly with concurrent PCS symptoms (King, 1996). In another, there were large group differences on measures of anxiety between a group with or without PCS (Meares et al., 2006). In addition to anxiety, depression also predicts PCS (Lange, Iverson, & Rose, 2011). PCS and emotional distress were highly correlated in a sample of mTBI and trauma control patients (Landre, Poppe, Davis, Schmaus, & Hobbs, 2006). In addition to the effects of concurrent affective disturbance, pre-injury psychiatric

diagnosis predicts the development of PCS in mTBI patients (Meares et al., 2008). In a pediatric concussion sample, those with premorbid anxiety disorders scored significantly higher on all three factors of the PCSS than those without anxiety disorders (Joyce, LaBella, & Carl, 2014). The overlap in symptoms between PCS and anxiety disorders and the comorbidity between the two makes differential diagnosis difficult and may lead to an under-diagnosis of anxiety disorders in this population; despite these difficulties, however, anxiety is a common affective outcome of mTBI and described in detail below.

Anxiety

The majority of studies examining affective outcomes following mTBI find an increase in anxiety symptoms and/or anxiety disorders (e.g., Epstein & Ursano, 1994; Mooney & Speed, 2001). However, some early studies did not find any evidence of anxiety following mTBI. For example, a study by Schoenhuber and Gentilini (1988) screened 35 head injured patients with the State Trait Anxiety Inventory at 5-17 months post-injury and found that there were no differences in either the state or trait subscale between patients and healthy controls. This lack of finding may be due to the small sample and the long post-injury periods seen in this study; it may be the case that any acute changes in anxiety resolve over a period of time. Some recent studies have found elevated levels of anxiety symptoms and disorders following mTBI. According to Rao and Lyketsos (2002), the most common post-TBI anxiety symptoms include “free-floating anxiety, fearfulness, intense worry, generalized uneasiness, social withdrawal, interpersonal sensitivity, and anxiety dreams.” In a meta-analysis, Epstein and Ursano (1994) found a prevalence rate of 23% for anxiety disorders in mild TBI across three studies; this statistic was slightly lower than the prevalence rate of 29% across all severity

of TBI across twelve studies. These statistics are consistent with those found by Mooney and Speed (2001) in which 24% of their participants with mild TBI were classified as having developed an acquired anxiety disorder. Within the general population, the pooled lifetime prevalence rate of anxiety disorders across 46 studies from 1980 to 2004 was 16.6% (Somers, Goldner, Waraich, & Hsu, 2006), suggesting that mTBI confers an increase in the likelihood of developing an anxiety disorder. As noted by Mainwaring, Hutchison, Camper, and Richards (2012) in a comprehensive review of the emotional sequelae of sports concussion, anxiety has not been a focus of study for investigators in this field. For example, while Erlanger and colleagues (2003) identified clinical reports of post-concussive irritability and nervousness following sports concussion, they did not examine symptoms of anxiety or the possible presence of anxiety disorders more specifically.

The prevalence of different types of anxiety disorders following TBI differ. Across all severity of TBI, 3-28% met the criteria for generalized anxiety disorder (GAD), 4-17% met criteria for Panic Disorder, 1-10% met criteria for phobic disorders, 2-15% met criteria for obsessive-compulsive disorder (OCD), and 3-27% met criteria for posttraumatic stress disorder (PTSD; Koponen et al., 2002; Hiott & Labbate, 2002). According to these data, the most prevalent forms of anxiety disorders following TBI are GAD, PTSD, and panic disorder. Within the general population, community lifetime prevalence rates for various disorders are estimated to be: 5% for GAD, 8% for PTSD, 1-2% for Panic Disorder, 4-8.8% for Specific Phobia, and 2.5% for OCD (DSM-IV-TR). When community prevalence rates are compared with prevalence rates for individuals following TBI, it appears that brain injury may confer a risk specifically for GAD, PTSD,

and Panic Disorder. Specific phobias and OCD do not appear to be significantly elevated following TBI.

With regard to mTBI in particular, research with military samples suggests that PTSD is particularly common after mTBI sustained during combat events. In a group of 2525 soldiers, 43.9% of those reporting a loss of consciousness met criteria for posttraumatic stress disorder (PTSD). In comparison, 27.3% of those reporting altered mental status, 16.2% of those reporting other injuries, and 9.1% of those denying any injury met the criteria for PTSD (Hoge et al., 2008). Other work has found similarly high rates of PTSD after mTBI (Bryant, 2001), and some studies suggest that combat-induced TBI approximately doubles the risk for PTSD (Schneiderman, Braver, & Kang, 2008).

The high degree of comorbidity that exists between PTSD and mTBI (Stein & McAllister, 2009) presents a number of difficulties for understanding their influence on one another. To begin, the differentiation between mTBI and PTSD is difficult due in part to the many overlapping and self-reported symptoms including fatigue, irritability, poor sleep, and a number of cognitive deficits. Differential diagnosis is therefore based largely on the predominant symptoms. Mild TBI is typically diagnosed on the basis of injury characteristics, including loss of consciousness, and posttraumatic amnesia and confusion, details of the injury itself (i.e. self and witness reports; Ruff, Iverson, Barth, Bush, & Broshek, 2009), and physical symptoms such as headache, difficulties concentrating, and photophobia and phonophobia. A diagnosis of PTSD is typically made on the basis of symptoms of re-experiencing, avoidance, negative mood and cognitions, and arousal (DSM-V). As a result, much controversy exists regarding the differentiation of mTBI and PTSD as well as their etiology. The problem of distinguishing between

mTBI and PTSD dates back to WWI and the concept of shell shock; at this time, there was much debate as to whether these symptoms represented psychic or physiological causes (Elder et al., 2012). Hoge and colleagues (2008) found a nonsignificant relationship between mTBI and outcome after controlling for PTSD, suggesting that poor outcome is the result of psychological variables and not lasting neurotrauma. In contrast, in a sample of trauma survivors, moderate to severe head injury and PTSD independently predicted symptom reporting and interacted such that the relationship between head injury and number of health complaints was stronger when posttraumatic stress disorder symptoms were more severe (Keatley, d'Alfonso, Abeare, Keller, & Bertelsen, 2015).

Other studies suggest that mTBI puts individuals at risk for developing PTSD. For example, Mora and colleagues (2009) studied 333 burn victims with or without primary blast injury/mTBI and found a greater prevalence of PTSD in those with mTBI than those with other injury mechanisms. Similarly, Walilko and colleagues (2009) examined 124 survivors of Oklahoma City Bombing and explored the relationship between PTSD and physical injuries; in this sample PTSD and head/brain injuries were significantly associated, while PTSD was not highly correlated with other injuries. These findings of Mora (2009) and Walilko (2009) suggest that TBI may predispose individuals to the development of PTSD. Bryant (2008) expanded on this idea and suggested that mild TBI may diminish the capacity to employ cognitive resources that would normally be engaged in problem solving and regulating emotions after trauma, thereby leaving individuals more susceptible to PTSD and related problems. Similarly, Elder and colleagues (2012) proposed that TBI might predispose individuals to PTSD if TBI damages brain structures involved in the development of PTSD. Specifically, current biological models of PTSD

identify frontal and limbic areas including the prefrontal cortex, amygdala, and hippocampus (Etkin & Wager, 2007). This is in keeping with neuroimaging findings in anxiety disorders that identify dysfunction in similar areas, including the amygdala, insula, and anterior cingulate cortex (Holzschneider & Mulert, 2011). Given that these medial brain regions are vulnerable to the effects of concussion, their dysfunction provides a possible biological mechanism for the increased risk for anxiety following concussion. One possible mechanism for this impact is through their influence on the hypothalamic-pituitary-adrenal (HPA) axis, which plays an important role in stress responses and anxiety. Another possible mechanism is through their purported role in classical conditioning, particularly fear conditioning.

Section I. Impact of Biological Variables: Aversive Conditioning and the HPA

The Role of the Hypothalamic-Pituitary-Adrenal (HPA) Axis

At a biological level, structures that play an important role in the regulation of responses to stress include the hypothalamic-pituitary-adrenal axis (HPA axis), brain stem noradrenergic neurons, sympathetic adrenomedullary circuits, and parasympathetic systems. The HPA axis is the neuroendocrine component of this stress response system. When a human perceives a stressful situation, the hypothalamus releases corticotropin-releasing factor (CRF)/corticotropin/releasing hormone (CRH). This then binds to CRF/CRH receptors on the anterior pituitary gland, signalling the release of adrenocorticotropic hormone (ACTH). Finally, ACTH binds to receptors in the adrenal gland to stimulate the release of glucocorticoids, including cortisol (Smith & Vale, 2006). The hypothalamus is regulated by glucocorticoid feedback, as well as by afferent projections from limbic (hippocampus, prefrontal cortex, amygdala), mid-brain, and brain

stem nuclei (Smith & Vale, 2006). The role of the HPA axis in stress, with stress often defined as a state of either real or perceived threat to homeostasis, has been well documented. In comparison, the role of the HPA axis in anxiety disorders has been less consistent. Whereas most research has found abnormal functioning of the HPA axis in these disorders, both overactivity and underactivity have been demonstrated (Gunnar, 2001; Vreeburg et al., 2010; Vreeburg et al., 2013) at baseline and in response to stressors. While underactivity may seem counterintuitive, some authors have suggested that this reflects an underlying exhaustion of the HPA axis (e.g., Vreeburg et al., 2013). Given the vulnerability of brain regions known to influence the HPA axis following mTBI, it may be hypothesized that dysfunction in these areas would have an impact on cortisol levels and cortisol-related stress responses in this group. In their study of psychological and physiological markers of stress in concussion, Hutchison, Mainwaring, Senthinathan, Churchill, Thomas, and Richards (2017) examined salivary cortisol as a potential biomarker of concussion across three time points of recovery and found no differences between concussed athletes and matched controls at any of the three time points, or over assessment time points. They did, however, find that salivary cortisol was correlated with a measure of perceived stress in the concussed athlete group. The authors suggested that this lack of sensitivity of cortisol to concussive injury may be due to the fact that it needs to be captured earlier post-injury. They also noted that, given its relationship to measures of self-reported stress, it may still be a useful marker for those concussed athletes that demonstrate persistent symptoms of stress. Despite a lack of differences in salivary cortisol levels at rest, concussed athletes may show a greater

cortisol-related stress response to experimental stressors or aversive conditioning procedures described in more detail below.

Aversive Conditioning and the Fear Circuit

The Relationship between Fear and Anxiety

Fear and anxiety are distinct, albeit closely related, concepts. Similarities between the two concepts include their main function and resulting autonomic responses. Specifically, both fear and anxiety serve to act as a signal of danger, threat, or motivational conflict. Accordingly, resulting physiological responses to both states involve the activation of the autonomic nervous system and corresponding arousal (Steimer, 2002). Fear and anxiety can be differentiated based on the object of danger or threat. In a fear state, the object of threat is real, external, and immediate. In contrast, feelings of anxiety are characterized largely by a sense of uncertainty; the possibility of danger is unknown and in the future. Fear diminishes once the object is removed, while anxiety often lasts longer. Both are generally adaptive, but anxiety can become maladaptive when it interferes with daily functioning, causes distress, and is excessive and long-lasting. Steimer (2002) described fear as a basic emotion, and anxiety as an elaborated form of fear that has evolved to help us plan and prepare for future danger or threat.

Despite the fact that humans possess a propensity for fear and anxiety and the fact that some fears and anxieties are innate, the majority are learned. For this reason, learning processes play a critical role in the emergence of both fear and anxiety. One particular form of learning that has been demonstrated to play an important role in the learning of anxiety is aversive conditioning, a form of associative conditioning.

Classical Conditioning

Pavlovian/classical conditioning is a form of associative learning in which a neutral stimulus and an unconditioned stimulus (US) are repeatedly paired together. After a number of trials, an association is learned between the neutral and unconditioned stimulus. The neutral, or conditioned (CS), stimulus can now elicit the unconditioned response (UR), now known as the conditioned response (CR), on its own. Extinction of a conditioned response occurs when the CS is no longer paired with the US; the conditioned response gradually diminishes over a number of trials in which the CS is presented on its own. Of note, this response does not reflect "forgetting," but rather a new form of learning in which the old response is inhibited. Another aspect of classical conditioning is the concept of generalization, in which conditioned responses are observed to novel stimuli that resemble the conditioned stimulus.

Fear learning is a subtype of classical conditioning that represents a rapidly acquired and generally adaptive form of associative learning and memory whereby we learn to fear certain places, people, and objects due to their association with feared stimuli. This form of learning is thought to play significant role in promoting survival from an evolutionary perspective. In aversive/fear conditioning a conditioned stimulus is paired with an unconditioned stimulus that is unpleasant (e.g., electric shock, loud noise) and the conditioned response may manifest in physiological, behavioural, or affective changes that reflect a fear response (Davey, 1992).

Conditioned fear responses vary by species and include physiological (i.e., increased heart rate), behavioural (i.e., freezing, avoidance), and affective (i.e., change in liking of the stimulus) responses. The learning of these associations can be assessed by

signal based and affective based measures (Neumann & Waters, 2006). Signal based or expectancy measures reflect learning of the association between the unconditioned and conditioned stimulus and may include expectancy ratings or physiological responses, including skin conductance and heart rate. Some studies have also used reaction time as a measure of associative learning (Craddock, Molet, & Miller, 2012). This type of learning may also be reflected in avoidance behaviours typically associated with anxiety disorders. Affective based measures reflect evaluative learning, which is observed as a change in the liking of a stimulus based on its association with other stimuli and may include subjective ratings of pleasantness, arousal, and interest of the stimuli, or startle blink reflexes, which may be mediated by the affective properties of a stimulus.

Although the typical unconditioned stimulus in aversive conditioning paradigms is a shock, this may not be appropriate for certain populations and is also limiting due to its high cost. Alternatives include a loud tone (typically 100-105 dB), unpleasant odour, and air puffs (Neumann & Waters, 2006). The most commonly used method in humans is the loud tone. However, recent research has also suggested the possibility of using sound stimuli that are aversive not because of their sound intensity but because of their inherent psychoacoustic properties (Vaschillo et al., 2003; Vaschillo, Vaschillo, Bergen, McLaughlin, & Servatius, 2003). Research of these acoustic properties demonstrated that a variety of modulated and unmodulated environmental sounds as well as artificially synthesized sounds can be unpleasant when presented at intensity levels of less than 82dB, which falls in the normal range for environmental sounds. In the acute phase of concussion recovery, phonophobia is a common symptom (Henry et al., 2010), possibly making an unconditioned stimulus presented at a lower volume a better choice.

Neumann and Waters (2006) examined whether this type of aversive sound could replace electric shock or loud noise in an aversive conditioning procedure. In two separate experiments with undergraduate students, the authors demonstrated that there were equivalent or superior conditioning effects in signal-based learning measures of US expectancy, skin conductance responses, and heart rate, and similar outcomes in affective-based learning measures of startle blink modulation and pleasantness ratings when a 3-second recording of a 3-pronged fork scraping over slate was used as an unconditioned stimulus.

Regardless of the type of stimuli used, fear conditioning has been examined extensively in the acquisition, maintenance, and extinction of anxiety disorders. Less research has focused on appetitive conditioning, a type of classical conditioning that involves the pairing of a pleasant and neutral stimulus. This type of conditioning has been less extensively studied, particularly within human populations, and the research with non-human animals has typically relied on the use of food as a positive, or rewarding, stimulus. Brain regions implicated in appetitive conditioning include the amygdala, orbitofrontal cortex, anterior cingulate, and striatum, suggesting at least some overlap in brain circuitry between aversive and appetitive conditioning (Martin-Soelch, Linthicum, & Ernst, 2007). Martin-Soelch, Linthicum, and Ernst (2007) did, however, note inconsistencies in amygdala activation during appetitive conditioning in humans, indicating that whereas some neuroimaging studies showed activation, others did not. The small body of research examining the implications of dysfunctional appetitive conditioning on psychiatric conditions has focused largely on substance abuse and eating disorders (e.g., Andreatta & Pauli, 2015; Martin-Soelch, Linthicum, & Ernst, 2007), and

not on anxiety disorders. It may be hypothesized, however, that given the reliance of both of these types of conditioning on similar brain networks, differences in at least some aspects of conditioning would be seen following disruption to these areas, for example during the disruption seen following mTBI or the dysfunction associated with anxiety disorders.

The Role of Aversive Conditioning in Anxiety

As noted previously, abnormalities in aversive conditioning have been demonstrated in both the acquisition and maintenance of anxiety disorders, with research in this area beginning in the early 1900s (Watson & Rayner, 1920). Whereas early theories focused on dysfunction in simple classical conditioning as the pathogenesis for anxiety disorders, later expansions involved more complex ideas, including the evolutionary benefit of easily learned aversive associations, the importance of conditioned fear in avoidance behaviours, stimulus generalization, and dysfunction of inhibitory systems in responding to safety cues. A renewed interest in the role of fear conditioning in anxiety disorders surfaced in the late 20th and early 21st century due to the introduction of more complex fear conditioning models and the investigation of the neural bases of fear conditioning in both human and non-human animal populations.

Aversive conditioning paradigms have also been used to examine differences between individuals with anxiety disorders and healthy controls. A quantitative review of the literature involving 20 studies demonstrated that anxious individuals demonstrate both significantly faster fear learning and more resistance to extinction than non-anxious controls, although these effects tend to be modest (Lissek et al., 2005). Importantly, these patient-control differences are not apparent when looking at discrimination or differential

conditioning studies; they emerge from studies that use simple, single-cue paradigms that require only a response to danger cues but no inhibition of fear to safety cues. Consistent with adult data, pediatric anxiety involves higher fear levels following simple conditioning procedures, but not greater differential conditioning (Lau et al., 2008).

In addition to examining differences between anxious and non-anxious individuals in general, fear conditioning paradigms have been employed to examine specific anxiety disorders. It has become a well-accepted paradigm for modeling the exaggerated and dysfunctional fear characteristic of PTSD (Iberzon & Sripada, 2008). Orr and colleagues (2000) found that individuals with PTSD showed elevated autonomic responses to aversive and novel stimuli associated with greater levels of fear acquisition and generalization, as well as reduced extinction of conditioned responses. A more recent study of individuals with posttraumatic stress symptoms following traumatic brain injury found stronger fear conditioning, but no differences in extinction (Glenn, Acheson, Geyer, Nievergelt, Baker, & Risbrough, 2017).

Aversive conditioning has also been examined in relationship to anxiety in healthy subjects (e.g., Buchel, Morris, Dolan, & Friston, 1998). This research has played an important role in our understanding of the functional neuroanatomy of anxiety (Holzschneider & Mulert, 2011). A study by Buchel et al. (1998) found that pairing a neutral face stimulus with an unpleasantly loud tone led to increased activation in the amygdala, insula, and anterior cingulate cortex when viewing the face alone, implicating these areas in an aversive conditioning network. A meta-analysis of fear conditioning/extinction studies using PET or fMRI imaging by Sehlmeyer and colleagues (2009) found evidence of similar regions of brain activation. Throughout these studies,

these brain regions were shown to be active during extinction as well as during acquisition of fear responses (Sehlmeyer et al., 2009). A review of studies using structural MRI, fMRI, and PET demonstrated activation of the fear network in addition to some prefrontal regions (Holzschneider & Mulert, 2011), suggesting a regulatory role of the prefrontal cortex on other structures of the fear network. The fear circuit is discussed in more detail in the following section.

The importance of learning in the development and persistence of anxiety disorders has been evidenced by the effectiveness of treating anxiety disorders with exposure-based therapeutic approaches (Lissek et al., 2005), as well as by the resemblance in functional neuroanatomy seen during both extinction procedures and the successful treatment of anxiety disorders (Holzschneider & Mulert, 2011). Fear conditioning paradigms exhibit considerable clinical relevance in both our understanding of anxiety disorders and in facilitating their treatment (Sehlmeyer et al., 2009). They may also provide a useful framework for understanding anxiety disorders following mild TBI if these processes are shown to differ between concussed and non-concussed groups.

Fear Circuit

A specific neural circuit underlying Pavlovian fear conditioning has been identified across studies. In rat populations, the amygdala, hippocampus, periaqueductal grey, and tegmental nuclei show increased activity during this type of associative learning (Fendt & Fanselow, 1999). Neuroimaging studies with human populations similarly indicate amygdala and hippocampal activity, as well as activity in additional brain areas, including the insula, anterior cingulate gyrus, and prefrontal cortical areas. A meta-analysis of studies using positron emission tomography or functional magnetic

resonance imaging suggested that a core network consisting of the amygdala, insula, and anterior cingulate cortex is activated independent of design parameters across fear conditioning studies. Other brain areas are recruited based on specific design parameters (Sehlmeyer et al., 2009).

The higher prevalence of anxiety disorders following mild TBI may be due partially to disruption in these cortical areas, particularly if these areas are implicated in the etiology of anxiety disorders in non-brain-injured individuals. As discussed earlier, recent work with rodent models of head injury suggest that many of these areas, particularly the amygdala, hippocampus, and prefrontal cortex, are indeed vulnerable to the neurometabolic and biomechanical effects of concussion. These brain structures are also implicated in the regulation of the HPA axis, which represents the neuroendocrine response to stress. In the subsequent sections, the role of each of these brain regions in fear conditioning and the pathogenesis of anxiety disorders is reviewed.

Amygdala

The importance of the amygdala in emotional processing is well-established. In the late 19th and early 20th century it was discovered that temporal lobe resections in monkeys resulted in loss of fear (Kluver and Bucy, 1939). Similarly, Weiskrantz (1956) identified a loss of fear due to temporal lobe damage, and connected this to damage in the amygdala specifically. Research since then has consistently shown that amygdala damage leads to reduced fear. For example, amygdala damage impairs acquisition of avoidance responses and failure to recognize fear in facial expressions (Maren, 2001). In contrast, electrical stimulation or seizure leads to autonomic and behaviour change characteristic of fear (Maren, 2001).

The amygdala plays a critical role in the acquisition and expression of conditioned fear because it is intricately and widely connected to other areas of the brain through various afferent and efferent connections (Fendt & Fanselow, 1999). It receives input from all sensory modalities largely through the thalamus, as well as from polymodal sources that include the prefrontal cortex, perirhinal cortex, and hippocampus. The basal nucleus is the main target of afferents from the prefrontal cortex. Many of these sources act in parallel and, in associative learning, carry information about the CS and US. The structure most directly implicated in CS-US associations is the lateral and/or basolateral amygdala (BLA), as evidenced by the fact that neurons in the BLA show short latency specific activity and increased responsiveness to stimuli after being paired with an US (Quirk, Repa, & LeDoux, 1995). The cellular mechanism underlying this learning seems to be NMDA receptor dependent long-term potentiation, as stimulation of afferent pathways to the amygdala lead to enhanced responsiveness of cells within the amygdala and glutamate receptors, particularly NMDA. Reger et al. (2012) suggested that normal fear conditioning processes in the amygdala are dependent on the optimal balance of inhibitory systems mediated by GABA and excitatory systems mediated by NMDA. NMDA receptor subunits mediate different aspects of fear conditioning; NR1 subunits represent the overall number of receptor subunits, NR2A subunits are particularly important for fear expression, and NR2B is particularly important for memory formation (Reger et al., 2012).

The projections from the amygdala are similarly vast, with sensory information from the BLA controlling output of the central amygdala (CeA). There are substantial pathways to the medial temporal lobe memory system, prefrontal cortex, and striatum.

There are also projections to the hypothalamus and brainstem. These efferent pathways control conditioned reactions of different motor and autonomic systems, and are largely glutamergic in nature (Sah, Faber, Lopez de Armentia, & Power, 2003). These efferent pathways mediate the physiological, behavioural, and affective unconditioned and conditioned responses, which include behaviour (e.g., freezing, vigilance, startle), autonomic effects (i.e., blood pressure, heart rate, respiratory changes), and HPA changes (i.e., corticosteroid release).

Overall, the amygdala acts as an interface between information from sensory modalities and the output of motor and autonomic systems. Its dysfunction has been linked to anxiety disorders in general. Specifically, amygdalar hyperactivity has been observed in the majority of functional neuroimaging studies investigating anxiety disorders (Holzschneider & Mulert, 2011; Etkin & Wager, 2007) these studies typically employed a symptom provocation paradigm where negative emotional conditions were contrasted with neutral or positive conditions. For example, negative emotional conditions included pictures of angry faces for individuals with social anxiety disorder (Klucken et al., 2009), trauma-related scenes or sounds for individuals with PTSD (Bremner et al., 1999), or pictures of spiders for individuals with specific phobia (Schweckendiek et al., 2011). The anxiety specific brain activity is then contrasted between individuals with anxiety disorders and healthy controls. One of the most consistent findings of brain activity is hyperactivity within the amygdala during symptom provocation. Amygdalar hyperactivity is posited to play a role in the persistently elevated fear response (Deckersbach, Dougherty, & Rauch, 2006) seen in PTSD. Simmons and Matthews (2012) conducted a meta-analysis that found increased activation in the

amygdala during affective and cognitive tasks in samples of PTSD patients. Similarly, in individuals with trait anxiety, there was increased amygdala responsivity to phasic fear cues in a fear conditioning paradigm (Indovina, Robbins, Nunez-Elizalde, Dunn, & Bishop, 2011).

Thy1+ neurons are a subpopulation of glutamergic pyramidal neurons in BLA involved in fear processing; specifically they are fear-suppressing neurons that are important for the extinction and inhibition of fear (Jasnow et al., 2013). When this subpopulation of neurons is activated during CS-US pairings, memory of these pairings is inhibited, thus inhibiting fear consolidation. Further, when these neurons are activated during extinction trials, there is enhanced extinction of the CS-US association. It can be hypothesized then, that a decrease in these neurons seen following mild TBI would be associated with increased fear consolidation and decreased extinction.

Research suggests that there may be specific proteins in the amygdala and hippocampus that mediate fear conditioning effects. For example, stathmin 1 is a protein abundant in the amygdala, particularly in the lateral nucleus where US and CS information converge, as well as in thalamic and cortical structures that send this information to the lateral nucleus (Elder et al., 2012). Knock-out models in mice show that the absence of this protein leads to deficits in spike-timing dependent long-term potentiation (Shumyatsky et al., 2005), which suggests that elevation of the levels of this gene would increase long-term potentiation and strengthen fear conditioning effects, consistent with the result of Elder and colleagues (2012). Stathmin 1 is known to influence the generation of fear responses for both innate and learned fear, as evidenced

partially by decreased memory in amygdala dependent fear conditioning in knockout mice (Shumyatsky et al., 2005).

Overall, the amygdala plays an important role within the fear circuit through its involvement in the acquisition of fear associations, as well as its role in the behavioural expression of this learned fear response. It has also been strongly implicated in anxiety disorders with neuroimaging studies demonstrating hyperactivity of the amygdala in individuals with these disorders.

Hippocampus

The hippocampus is also a part of the fear circuit and plays an important role in emotional responding and human memory, particularly spatial memory. Fendt and Fanselow (1999) and Reger et al. (2012) discuss the important role of the hippocampus in the neural circuitry of fear, particularly as it relates to the contextual tagging of fear responses (Vasterling, Verfaellie, & Sullivan, 2009). The identification of safe contexts is mediated by the hippocampus and dysfunction in this process is suggested by hippocampal hypoactivity in PTSD patients (Hayes, et al., 2011). Reger and colleagues (2012) indicated that GABA plays an important role in both the amygdala and hippocampus for normal fear conditioning. Neuroimaging in individuals with PTSD compared to healthy controls specifically has shown hypoactivity in the hippocampus (Deckersbach et al., 2006), as well as atrophy of the hippocampus as evidenced by bilateral smaller volume (Smith, 2005).

Prefrontal Cortex

Neuroimaging and animal models of anxiety consistently demonstrate abnormalities in prefrontal cortical functioning. Studies suggest that frontal lobe

dysfunction can cause emotional symptoms by reducing the capacity of an individual to adapt to environmental change (Simmons & Matthews, 2012). Neural models of PTSD posit that PTSD-like symptoms are related to ineffective top-down modulation of the amygdala and limbic circuitry by the prefrontal cortex (Liberzon & Sripada 2008; Shin, Rauch, & Pitman, 2006), resulting in a reduced potential for top-down processes in the regulation of fear learning (Deckersbach et al., 2006).

Individuals with high trait anxiety have hypoactivity in the ventral prefrontal cortex (vPFC) during both cued and contextual fear (Indovina et al., 2011). A meta-analysis by Simmons and Matthews (2012) found decreased activation in those with PTSD compared to controls in anterior cingulate and medial frontal gyrus during affective tasks. There is some consistency with other PTSD neuroimaging studies that have shown hypoactivity in the anterior cingulate gyrus, but also in the medial prefrontal cortex (mPFC; Shin et al., 2006; Etkin & Wager, 2007). Differential patterns of activation may be attributed to a number of factors, including task characteristics; however, there does appear to be some consistency in decreased activation in medial prefrontal regions generally.

The mPFC plays an important role in behavioural inhibition as neuronal pathways from the mPFC inhibit central amygdala nucleus output, as well as input from the insula and BLA. Inhibition is a critical aspect in extinction processes. (Quirk & Beer, 2006). Evidence of the mPFC's role in fear extinction comes from a number of sources, including impaired extinction following lesions of the mPFC, the correlation of mPFC potentiation and extinction, and the strengthening of extinction following stimulation of the mPFC (Quirk & Beer, 2006). Further, in individuals suffering from PTSD, areas of

mPFC show morphological and functional abnormalities (Nutt & Malizia, 2004; Liberzon & Sripada, 2008). Thus, the prefrontal cortex appears to play an important role in the top-down regulation and inhibition of other areas within the fear circuit.

Insula

The insula receives and integrates sensory, homeostatic, motivation, emotional, and cognitive information from a variety of cortical and subcortical regions; as such, it is involved in the perception of subjective interoceptive states and emotional awareness (Grupe & Nitschke, 2013). Hyperactivity of this brain region is consistently associated with anxiety. In a sample of anxiety-prone individuals, there was increased activity in the insula during the presentation of emotional faces in comparison to controls (Stein, Simmons, Feinstein, & Paulus, 2007). Further, hyperactivity within the insula has been shown in a number of anxiety disorders, including PTSD, social anxiety, and specific phobia (Etkin & Wager, 2007; Grupe & Nitschke, 2013). Finally, this area also shows hyperactivity during fear conditioning in healthy controls (Etkin & Wager, 2007; Grupe & Nitschke, 2013).

Overall, the fear circuit consists of complex interplay between a number of brain regions, including the amygdala, hippocampus, prefrontal cortex, and insula. Given the vulnerability of these areas to mTBI and their role in fear conditioning, dysfunction in this network may lead to abnormal associative learning and increased risk for anxiety disorders following mTBI.

Role of the Traumatic Event

The majority of studies of fear conditioning following mTBI in humans have been conducted in veteran or soldier populations. However, concussed athletes may provide a

complimentary population in which to examine the effect of mTBI on subsequent aversive conditioning as the majority of sports-related concussions are arguably less stressful than those sustained in combat, motor vehicle accidents, or falls, and that certain protective personality traits, including a lower incidence of premorbid psychiatric comorbidities, may be more common among athletes (Rabinowitz et al., 2014). Thus, any changes in aversive conditioning following mTBI in this population would more clearly delineate pathophysiological effects of brain injury with less of the confounding emotional distress that is associated with other causes of mTBI.

Many researchers employing mTBI procedures in rodents have recognized this inherent difficulty and have used a number of stress-alleviating procedures. At the very minimum, these studies have used anaesthesia during brain injury procedures (e.g. Genovese et al., 2013). Other work has employed more stringent protocols for reducing emotional distress; Almeida-Suhett and associates followed strict stress-mitigating guidelines that involved an acclimation period of at least 3 days prior to experimental procedures, having cages cleaned only once per week, minimization of handling, and the provision of pain-alleviating medication. These studies of rodent models have provided most of the current information on fear conditioning following mTBI, and are summarized below.

Rodent Models of Aversive Conditioning following mTBI

Within the framework of brain injury in rats, researchers have examined anxiety-like behaviours (Meyer et al., 2012; Elder, 2012) and conditioned fear (Meyer et al., 2012; Elder, 2012; Lifshitz et al., 2007), including acquisition, generalization, and extinction. Lifshitz et al. (2007) found hippocampal (spatial learning), but not amygdala-

dependent cognitive deficits 7-days post-injury that resolved by 1-month post-injury. Specifically, conditioned fear response was observed to the trained context but not to the trained cue. The cognitive deficits were related to deficits in conditioned context, which is mediated by the hippocampus, but not conditioned cues, mediated by the amygdala. Genovese and colleagues (2013) used a conditioned fear procedure within an operant conditioning paradigm and found a decrease in conditioned fear responding; specifically, rats exhibited less suppression of an operantly conditioned behaviour in the presence of a conditioned stimulus. The authors interpreted this finding as reflecting changes in inhibitory systems following brain injury. Most studies, however, have found increases in conditioned fear and anxiety behaviours.

Reger et al. (2012) found increases in fear conditioning, regardless of whether the response was retrieved via discrete (cued) or contextual (spatial) stimuli 2 days post-injury. This study also found overgeneralization of the fear response to both conditioned and novel stimuli. Almeida-Suhett et al. (2014) used an open-field test 1, 7, and 30 days post-injury and found increases in anxiety behaviours as indicated by significantly less time spent in the center at 7 and 30 days post injury without any associated differences in distance traveled or total movement time. Elder and colleagues (2012) studied the behaviour of rats exposed to repetitive blast injury and found that these injuries induced a number of PTSD-related behavioural traits, including increased anxiety, enhanced contextual fear conditioning, and an altered response in a predator scent assay. Meyer and colleagues (2012) reported that mTBI increased expression of anxiety-like behaviors and conditioned fear, with no effect on motor performance or nociception. Heldt et al. (2014) found that overpressure air blast in rats produced anxiety-like behaviour, specifically

lingering in the middle of an open field arena, increased acoustic startle, diminished prepulse inhibition (PPI; the inhibition of a reaction to a strong stimuli when preceded by a subthreshold stimulus), increased contextual fear, and perseverance of cued learned fear over a 2-8 week period after the blast procedure. In a study of mice exposed to 50-psi blasts, there was a significant increase in learned contextual fear as compared to sham mice (Reiner et al., 2015). Further, mice undergoing 50-psi blasts also showed a large and significant overall increase across trials in conditioned freezing responses to the conditioned stimulus (CS).

Overall, significant changes in anxiety behaviours and fear conditioning, generalization, and extinction following experimentally induced mTBI have been demonstrated. These models have not yet been tested in human mTBI populations. Thus, possible changes in these processes and behaviours in individuals following concussion when the brain may be more vulnerable to acquisition of aversive learning were examined in the present study. As suggested by King (2003), organic factors such as these can be particularly important in the acute phase following head injury; however, the importance of psychological variables becomes increasingly important beginning as early as 24 hours after an injury. These psychological factors may include the individual's perception of the injury and the coping mechanisms initiated to cope with the cognitive and emotional representations of the injury.

Section II. Impact of Psychological Variables: Illness Representations and Coping

Common Sense Model

The Common Sense Model (CSM; Leventhal, Leventhal, & Contrada, 1998) is one of the most influential psychological frameworks in the understanding of health and

illness outcomes. The research that led to the development of this model began in the 1960s and 1970s with a series of studies examining fear communications and action plans in health attitudes. Since that time, it has been applied in the understanding of a variety of illnesses, syndromes, and injuries (e.g., Hagger & Orbell, 2003). The CSM is based on the idea that individuals form illness representations that guide them in interpreting and coping with a given illness, disease, or injury. Within this framework, the individual is conceptualized as an active problem solver dealing with the parallel processing of both cognitive and emotional illness representations. This model has three central tenets: 1) the individual is seen as an active problem solver, seeking out information and testing hypotheses about symptoms, 2) illness representation is the central cognitive construct and is conceptualized to guide coping responses and appraisal processes, and 3) there is a highly individualized nature to illness representations, meaning that they are not necessarily factual in nature (Diefenbach & Leventhal, 1996).

Illness representations are constructed from three major sources of information: "lay" information, including media sources; information from external sources including parents, friends, and medical professionals; and the individual's experience with the illness, both past and current. Illness representations can be cued by both internal cues, such as symptoms, and external cues, such as a media campaign. Sources of information may be either concrete (i.e., personal experiences or memories) or abstract (i.e., knowledge regarding causes of a particular illness) in nature.

The CSM is conceptualized as a hierarchical system featuring three major constructs: 1) illness representations that guide, 2) coping responses, and 3) subsequent appraisals that monitor the success or failure of the coping responses (Nerenz &

Leventhal, 1983). Appraisals can lead to new cognitive and emotional illness representations, creating a feedback loop within this model. Outcomes are thus influenced by illness representations that lead to specific coping strategies. The independent effects of illness representations and coping strategies as well as their interaction are detailed in the following sections.

Components of Illness Representations

Based on qualitative studies employing open-ended interviews (Linz, Penrod, & Leventhal, 1982; Meyer, Leventhal, & Gutmann, 1985), five core components of illness representations have been identified: identity, cause, timeline, consequences, and controllability. Identity refers to a given disease or illness label and knowledge about the associated somatic representations (i.e., symptoms). The causal attribution includes beliefs about the causal factors responsible for the illness or injury. Causes are vast in nature, but have been put into a limited number of dimensions based on factor analytic studies. These include biological, emotional, environmental, and psychological. There is clearly some overlap in these dimensions (e.g., depression could be both emotional and psychological), making some findings using this classification system difficult to interpret. As a result, some studies use a single item measure of each dimension. Causes can also be classified as internal or external. One measure of illness representations, the Illness Perception Questionnaire - Revised (IPQ-R; Weinman, Petrie, Moss-Morris, & Horne, 1996) uses four dimensions of causal attributions, including psychological attributions, such as personality, stress, or worry; risk factors, such as heredity or smoking; immunity like germs or viruses; and accident or chance. The timeline dimension refers to beliefs about the expected timeframe of the injury or illness. It

distinguishes between acute and chronic, as well as cyclical or persistent illnesses. The consequences dimension includes an individual's beliefs about the impact of the illness on their daily life, including their quality of life, functioning, emotions, and finances. Finally, the controllability dimension refers to an individual's beliefs about the efficacy of both their coping efforts and their treatment regimen.

Illness representations comprise both the cognitive representations just discussed as well as emotional representations. Emotional responses to injury or illness-related stimuli are activated in association with cognitive representations. These emotional representations may include symptoms of anxiety, depression, stress, annoyance, or fear, and can be modified by cognitive processes. For example, similar symptoms may lead to different emotions based on their appraisal. The type of emotion evoked by the injury can influence the coping choices made and subsequent affective outcomes. A number of coping strategies may be applied simultaneously to address the varying cognitive and emotional aspects of the illness representation.

Applying the illness representations concept of the CSM has been helpful in understanding health outcomes in a range of conditions, including chronic fatigue syndrome (Moss-Morris, Petrie, & Weinman, 1996), asthma (Horne & Weinman, 2002), and diabetes (Skinner & Hampson, 1998). Only a limited number of studies have evaluated the CSM in the context of mild TBI in athletes and patient groups (Whittaker, Kemp, & House, 2007). Some studies have examined illness perceptions in athletes with a range of injuries. For example, Hagger, Chatzisarantis, Griffin, and Thatcher (2005) explored the effect of injury representations on outcome in athletes with sports-related muscoskeletal injuries. Within this sample, both negative and positive affect were

influenced by injury beliefs, specifically emotional representations. In addition to emotional representations, other aspects of illness perceptions, including identity, serious consequences, and causal attributions predicted functioning in athletics. Finally, injury severity, identity and personal control predicted attendance at treatment centers. In keeping with the meta-analysis conducted by Hagger and Orbell (2003), a study by Van Wilgen, Kaptein, and Brink (2010) found that athletes with a diverse range of injuries were shown to generally possess a weak illness identity and high controllability. These athletes viewed their injury as having an acute timeline and related minimal consequences to their injury. They did not exhibit a high emotional representation of their illness. They generally possessed a strong understanding of their symptoms and injury (high illness coherence), along with high levels of personal and treatment control. As injuries became more long-lasting in nature, athletes in this study exhibited more chronic timeline beliefs, but attributed their injury to fewer psychological causes.

A few studies have explored the role of illness perceptions in outcome for mild TBI groups. Whittaker and colleagues (2007) examined 73 patients with a mild head injury at 3-months post-injury. On the measure of illness representations employed, beliefs about timeline and consequences were important variables in predicting PCS. Specifically, patients with stronger beliefs about the seriousness and enduring nature of the consequences of mild TBI were at increased risk for PCS. In this study, measures of distress, including anxiety and depression, were not predictive of PCS. Snell and colleagues (2011a) examined 147 patients who presented to a concussion clinic or emergency department setting with a mild TBI 3-months post-injury. Significant associations between poor outcome, conceptualized as number of PCS symptoms, and a

number of illness beliefs were demonstrated. A greater endorsement of symptoms related to the injury, the severity of injury-related consequences, the chronicity and unpredictability of symptoms, and less understanding of the condition were associated with poor outcome. In addition, there was a significant relationship between poor outcome and emotional representations. These patients were examined again at 6-months post-injury (Snell, Hay-Smith, Surgenor, & Siegert, 2013) and similar associations were found; participants with greater injury identity beliefs and expectations of lasting severe consequences were at risk of poor outcome. Contrary to the study by Whittaker and colleagues (2007), levels of psychological distress were associated with outcome in this sample, both at 3-months and 6-months post-injury. Overall, these groups reported an important role for illness perceptions in outcome following mild forms of brain injury. However, they have typically conceptualized outcome in terms of lasting concussion symptoms and the development of PCS. None of these studies have examined the role of illness perceptions in the acquisition of anxiety disorders following injury.

The role of cognitive representations, specifically symptom attribution and associated outcome expectation, has also been studied outside of the CSM. Examination of the effects of symptom attribution has been varied experimentally using “diagnosis threat,” a type of stereotype threat in which individuals are made aware of their membership in a specific group (e.g., individual with concussion) and then given a task or asked questions that have specific stereotypes associated with that group. Within this model, experimental participants are put into a threat position by being informed that their concussion is the subject of study. Using this framework, Suhr and Gunstad (2002) found that a diagnostic threat group performed worse on tests of neuropsychological

performance and reported that they put forth less effort than did a neutral group not informed that their injury was under study. An investigation of the self-reported nature of these attributions in a group of veterans (Larson, Kondiles, Starr, & Zollman, 2013) found that strong symptom attribution (i.e. believing that symptoms were caused by the concussion) was associated with increased symptom report. Ozen and Fernandes (2011) created four groups: mild head injured (MHI) individuals with diagnostic threat, controls with diagnostic threat, MHI individuals without diagnostic threat, and controls without diagnostic threat. MHI individuals in the diagnostic threat condition self-reported more attention problems than both controls with diagnostic threat and neutral MHI individuals. They self-reported more memory failures than diagnostic threat controls. On neuropsychological testing, MHI individuals performed worse on tests of attention span regardless of group. Measures of depression and anxiety were also examined within this group. There were differences between the groups on a measure of self-reported depressive symptoms, but MHI individuals in the neutral group reported more state and trait anxiety symptoms than control neutral participants. They also reported higher anxiety levels than the diagnostic threat MHI individuals, possibly due to the fact that the individuals in the diagnostic threat group felt they were given a justification for their poor cognitive performance. It may be hypothesized that the effect of diagnostic threat on anxiety would be different if individuals were instructed that the impact of concussion on affective symptoms was being examined.

Coping

Coping can be defined as the "constantly changing cognitive and behavioural efforts to manage specific external and/or internal demands that are appraised as taxing"

(Lazarus & Folkman, 1984). Within their theory of stress and adjustment, a situation is defined as stressful by an individual's unique appraisal of a situation, not the objective characteristics of the situation. When the subjective demands of a situation are appraised as exceeding an individual's coping resources, emotional distress is experienced. Once this appraisal has been made, coping strategies are employed. Within this broad definition, numerous specific types of coping strategies can be identified, including active coping, seeking social support for instrumental or emotional reasons, mental or behavioural disengagement, and denial (Tomberg, Toomela, Pulver, & Tikk, 2005).

At a more general level, coping strategies can be classified as either adaptive or maladaptive in nature. The dispositional approach of coping suggest that coping strategies fall under three main categories of task-oriented, social/emotional, and avoidance oriented strategies, with task-oriented approaches typically being the most functional. Other classification systems are slightly different, categorizing coping strategies as problem-focused, emotion-focused, or social (Tomberg et al., 2005). This type of classification systems fits well with the Common Sense Model, where illness representations are constructed at both cognitive and emotional levels. Problem-focused strategies typically deal directly with the situation itself by obtaining more information or skills to manage the situation (self-focused) or by changing the environment (environment focused). Emotion-focused strategies focus on changing the way in which the individual attends to the situation (avoidance or denial) or altering the individual's subjective appraisal of the situation (positive reappraisal or acceptance; Lazarus, 1993). It can also be useful to classify coping strategies as either engagement or disengagement

strategies, depending on whether the response is active or passive in nature (Tomberg et al., 2005).

Within the Common Sense Model, illness representations guide the selection and employment of coping strategies. A meta-analysis of the Common Sense Model across a wide range of illnesses tested this hypothesis and provided some support for this relationship (Hagger & Orbell, 2003). Specifically, the authors found that individuals reporting more symptoms (i.e., higher identity beliefs) and individuals believing that the illness had significant consequences were more likely to use avoidance/denial and emotion expression as coping strategies. Patients who viewed their illness as more chronic in nature were also more likely to use avoidance/denial in addition to cognitive appraisal strategies. Finally, individuals with greater endorsement of control over the illness were more likely to use adaptive coping strategies, such as problem-focused coping, cognitive reappraisal, and seeking social support.

The importance of coping strategies following TBI is exemplified by studies demonstrating an association between coping strategies and emotional outcome 1-5 years later in individuals who have suffered an insult to the brain (Curran, Ponsford, & Crowe, 2000). Finset and Andersson (2000) found that certain coping strategies were associated with different types of emotional outcomes. Specifically, avoidant coping strategies were associated with increased rates of depression, while a lack of active approach-oriented coping was associated with apathy. Not only are negative coping strategies associated with poor outcome, but adaptive coping techniques actually appear to play a protective role in TBI (Tomberg et al., 2005). Further evidence comes from a study by Anson and Ponsford (2006) who investigated the relationship between coping and emotional

adjustment following TBI. In this sample, there was a strong association between style of coping used to manage stress and emotional adjustment. Specifically, coping characterized by avoidance, worry, wishful thinking, self-blame, and the use of drugs and alcohol was associated with higher levels of anxiety, depression, and psychosocial dysfunction, and lower levels of self-esteem; in comparison, coping characterized by actively working on the problem and the use of humour and enjoyable activities to manage stress was associated with higher self-esteem. In addition, the presence of TBI itself seems to have an impact on the type of coping strategies used. For example, Tomberg and colleagues (2005) found that individuals with TBI used less task-oriented and social-emotional support strategies, and more avoidance-oriented strategies than healthy controls. Within the TBI sample of this study, the use of task-oriented coping strategies was associated with positive outcomes, including health-related Quality of Life measures and return to work. It is important to note that the previously cited studies have included TBIs of all severities, ranging mostly from moderate to severe.

A small number of recent studies have examined the effects of coping in mild TBI populations specifically (Woodrome et al., 2011; Snell et al., 2011a; Covassin, Elbin, Crutcher, Burkhart, & Kontos, 2013). A number of these studies use concussed athlete populations, so the following section will begin with a look at coping strategies employed by athletes more generally.

In athlete populations in general, problem-focused coping strategies are common (Van Wilgen et al., 2010) and tend to be related to positive outcomes. For example, in a group of athletes with sports-related muscoskeletal injuries problem-focused coping predicted 3-week follow-up attendance (Hagger et al., 2005). According to a meta-

analysis conducted by Hagger and Orbell (2003), high controllability in athletes was significantly associated with cognitive reappraisal, expressing emotions, and problem-focused coping. Within athlete populations, there is evidence to suggest that coping responses following brain injuries may differ from those following orthopedic injuries. In line with this hypothesis, Kontos et al. (2013) found that concussed athletes reported employing fewer coping strategies overall than athletes with orthopedic injuries. Specifically, they reported lower levels of denial, substance abuse, behavioural disengagement, venting, planning, humour, religion, self-blame, self-distraction, and positive reframing. Of note, the majority of these coping strategies are maladaptive in nature. The lower levels of coping seen in the concussed athletes may be a result of the passive recovery demands following a concussion in comparison to the active recovery demands of an orthopedic injury. The impact of this pattern of reduced overall coping on outcome was not examined.

Additional research has been conducted to evaluate the relationship between type of injury, coping strategies, and outcome. For example, Woodrome et al. (2011) compared problem-solving and emotion-focused coping following mild TBI and orthopedic injuries (OI) in children. Within this study, problem-focused engagement strategies included problem-solving and cognitive restructuring, and problem-focused disengagement strategies included problem avoidance and wishful thinking. Emotion-focused engagement strategies included the expression of emotions and social contact, whereas emotion-focused disengagement strategies included self-criticism and social withdrawal. Self-ratings of symptoms were positively related to emotion-focused strategies and negatively related to problem-focused engagement after both mild TBI and

OI. Reports of emotion-focused engagement and disengagement strategies were positively correlated to number of symptoms in both the mild TBI and OI groups. Problem-focused engagement strategies were associated with fewer symptoms in both groups. However, the relationship between problem-focused disengagement and symptoms varied according to group. In the mild TBI group, problem-focused disengagement was associated with more symptoms, while in the OI group problem-focused disengagement was associated with fewer symptoms. The reasons for this finding are unclear, but the authors suggested that it may be related to the number of symptoms associated with mild TBI versus orthopedic injuries; specifically, it may be effective to avoid or deny the minimal consequences of an orthopedic injury, but ineffective with the persistent sequelae of a head injury.

Covassin and colleagues (2013) studied 104 concussed athletes and their coping strategies at both 3 and 8-days post-injury. These athletes reported greater use of avoidance coping, use of self-distraction, behavioural disengagement, religion, and self-blame at 3-days post-concussion than at 8-days post-concussion. Further, total number of reported symptoms was a significant predictor of avoidance coping 3 days post-injury. At 8-days post-injury, decreased visual memory was associated with increased avoidance coping, indicating a relationship between these coping techniques and poor cognitive outcome. However, the directionality of this relationship is unclear. Avoidance coping at this acute phase may represent an adaptive response to the passive nature of concussion rehabilitation; thus, increased symptoms and decreased visual memory may lead to a preference for these coping strategies.

Other researchers have examined coping strategies over longer periods of time following concussion. For example, Snell and colleagues (2011a; 2013) conducted a prospective study that examined 147 patients who presented to a concussion clinic or emergency department setting at two time intervals: within 3 months of injury (Time 1) and at 6-9 months post-injury (Time 2). At both time points, individuals were dichotomously classified as having either good or poor outcome based on number of symptoms, problems with activities and participation, and negative change in work status since the injury. Univariate analyses at Time 1 indicated an association between outcome and approach coping, specifically planning and positive reframing that approached statistical significance. At Time 2, those individuals in the poor outcome group had endorsed greater use of approach coping strategies at Time 1. The only association between outcome and Time 2 coping was with denial, in that greater use of denial strategies at Time 2 was associated with poor outcome. Snell and colleagues (2013) also examined changes in coping style over time between the good and poor outcome groups. Those in the good outcome group reported significantly greater use of certain approach coping strategies, including positive reframing and acceptance, as well as decreased self-blame. The opposite pattern was seen in the coping strategies of individuals in the poor outcome group.

The studies of Woodrome et al. (2011), Covassin et al. (2013), and Snell et al. (2011a) suggest that approach strategies are associated with poor outcomes early after injury when passive recovery is appropriate, while avoidance coping strategies are associated with poor outcome when the injury becomes chronic and more active coping may be necessary. The comparison of coping in concussed athletes and athletes with

other injuries suggests that this coping pattern may be specific to individuals with head injuries.

In an effort to integrate the findings of studies employing the CSM across various illnesses and diseases, Hagger and Orbell (2003) conducted a meta-analysis of 45 empirical studies working within this framework. Across illness types, a common pattern of predictable relations among cognitions, coping, and a variety of outcome variables emerged. Specifically, perceptions of strong illness identity were significantly and positively related to the use of coping strategies of avoidance and emotional expression. Perceived controllability of illness was significantly associated with cognitive reappraisal, expressing emotions, and problem-focused coping strategies. Perceptions of illness as being highly symptomatic, having a chronic timeline, and having serious consequences were related with avoidance and expressing emotions. Perceptions of illness as curable or controllable related to adaptive outcomes of psychological well-being, social functioning, and vitality, and were negatively related to psychological distress and objective measures of illness status or severity. Those who perceived their illness to have serious consequences, a chronic timeline, and a greater number of symptoms tended to score lower on adaptive illness outcomes, including psychological well-being, role and social functioning, and vitality.

Common Sense Model: A Mediational Model

Research using the CSM in the understanding of mild TBI has provided abundant evidence for the importance of both illness representations and coping strategies in predicting outcome. Despite the plethora of studies examining these independent effects, the literature is lacking in one specific aspect; namely, the interaction of these variables

in predicting outcome. As mentioned previously, the CSM is proposed largely as a mediational model, wherein coping mediates the relationship between illness representations and outcome. A recent review of the literature suggests that, although studies have examined aspects of the CSM in a mild TBI sample, no study explicitly examining the mediational relationships of this model in this population has been conducted to date.

The mediational relationship proposed by the CSM has been examined in a number of other injury and illness groups, including individuals with diabetes, allergies, rheumatoid arthritis, Parkinson's disease, and cancer. Whereas some have found no evidence to suggest that coping acts as a mediator (e.g. Edgar & Skinner, 2003; Rutter & Rutter, 2007), many studies have found evidence for at least a partially mediated relationship (e.g. Knibb & Horton, 2008; Carlisle, John, Fife-Schaw, & Lloyd, 2005; Evans & Norman, 2009; Gould, Brown, & Bramwell, 2010). In those studies finding a mediational relationship, avoidant types of coping were most often found to mediate the relationship between aspects of illness representations and outcome. For example, Carlisle, John, Fife-Schaw, & Lloyd (2005) found that avoidant and resigned coping partially mediated the relationship between symptom identity (i.e., number of symptoms reported) and disability and psychiatric outcome in a sample of women with rheumatoid arthritis.

Evans & Norman, (2009) found a slightly different role of avoidant coping; specifically, this type of coping played a mediation role between emotion representations of illness and anxiety outcomes in individuals with Parkinson's disease. Results of a study conducted by Gould, Brown, & Bramwell (2010) in a population of recently

diagnosed cancer patients suggested yet another role of avoidant coping, whereby denial and avoidant coping mediated the relationship between illness timeline beliefs and mood outcomes. The differences in these studies are likely related to different illness populations, and different measures of coping and outcome.

Despite the differences across studies, a mediating role of avoidant types of coping is apparent in the relationship between illness representations and outcome. Although the possibility that coping mediates the effect of illness representations on concussion outcome has not previously been investigated, evidence suggesting the possibility of this relationship is provided by the previously cited literature suggesting that: the purported independent variable (illness representations) is associated with the purported mediator (coping), and both have strong associations with outcome in mild TBI populations.

Current Study

The goal of the current study was to add to the body of literature examining outcome following mild TBI. The purpose of this study was two-fold. First, this study aimed to further the understanding of the increased vulnerability to acquired anxiety disorders seen following mild TBI. Recent research employing rodent models of head injury suggests that regions of the brain involved in fear conditioning demonstrate microstructural and functional changes following a blow to the head. Further, rodents exposed to a mild brain injury exhibit increased conditioning effects and anxiety-like behaviours. In this study, these findings are extended to a human population by comparing aversive conditioning in concussed individuals during the acute phase of recovery to control participants. Second, the CSM is used as a framework in which to test

a mediational model of outcome following concussion. Previous research using the CSM across illnesses and injuries has found some evidence for the role of coping as a partial mediator between illness representations and outcome. Some work has applied the CSM to mild TBI populations, but largely restricted to examining the independent effects of illness representations and coping strategies. A goal of the current study was to further the understanding of this model in head injury groups by examining a mediational model of illness representations, coping, and outcome in athletes at the acute phase of recovery. Specific hypotheses are as follows:

Hypothesis 1: Concussed athletes and controls will differ in their learning of the association between the conditioned stimulus (CS+) and the unconditioned stimulus (US), as demonstrated by higher average expectancy ratings, greater generalization, faster learning, and slower extinction in the concussed athlete group.

a. Athletes will exhibit higher average expectancy ratings to the CS+ in the acquisition, generalization, and extinction phases of the aversive task.
b. Athletes will demonstrate faster learning of the association between the US and the CS+ during the acquisition trial than controls, as evidenced by fewer trials to reach 100% expectancy.
c. Athletes will demonstrate slower extinction of the association between the US and the CS+ during the extinction trial than controls, as evidenced by more trials to reach -100% expectancy.
d. Athletes will be more likely to generalize to other stimuli, and will therefore show a higher generalization quotient of expectancy ratings than controls.

e. Exploratory analyses will examine possible differences between concussed athletes and controls in a pleasant conditioning task.

Hypothesis 2: Concussed athletes will demonstrate a greater autonomic stress response.

a. Athletes will exhibit greater heart rate responses and skin conductance responses to the CS+ than controls during the acquisition, generalization, and extinction phases.
b. Athletes will exhibit greater heart rate and skin conductance responses to generalization stimuli than controls.
c. Exploratory analyses will examine possible differences in heart rate and skin conductance response to the CS+ during a pleasant conditioning task.

Hypothesis 3: Athletes will demonstrate a higher cortisol-related stress response (i.e., cortisol levels will decrease less over time) than controls.

Hypothesis 4: Concussed athletes will demonstrate faster reaction times.

a. Athletes will exhibit faster reaction times to the CS+ than controls during the acquisition, generalization, and extinction phases.
b. Athletes will exhibit faster reaction times to the generalization stimuli than controls.
c. Exploratory analyses will examine possible differences in reaction time to the CS+ and generalization stimuli during a pleasant conditioning task.

Hypothesis 5: Avoidant coping will mediate the relationship between illness representations (both cognitive and emotional) and symptoms in the concussed athlete group. It is also hypothesized that the pre-requisite independent effects of both illness

representations and coping on outcome, as well as a significant association between illness representations and coping, will be present.

a. Based on hypotheses that recovery in the acute phase of a concussion requires more passive coping strategies, it is hypothesized that approach coping strategies will partially mediate poor outcome in this group.

CHAPTER 3

METHOD

Participants

The clinical population for this study included University of Windsor Varsity athletes (n = 16) referred to the Sport-Related Concussion Centre (SRCC) for a post-concussion evaluation due to suspicion of concussion based on an incident where there was an impact and associated cognitive (e.g., confusion, decreased concentration) or physical symptoms (e.g., headache, sensitivity to light or noise). This study was completed during the first years of the SRCC, a time during which referral methods and research recruitment strategies were being refined; as result, there were some delays in contacting and scheduling evaluations and research timeslots. The control population for this study consisted of University of Windsor non-athlete undergraduate students (n = 41) with no reported history of head injury. These participants were recruited through the Psychology Participant Pool.

The presence of a concussion in the clinical sample was based on self-reported history of a head injury and a referral from the athletic trainer for a post-injury evaluation. When an athlete was referred to the SRCC, they were called or e-mailed to set up an appointment for their post-injury evaluation. At this point, they were asked whether

they would like to participate in the ongoing research study. Compensation for the 1.5 hour study was initially $20, but increased to $50 due to low recruitment rates.

Exclusion criteria for the control participants in this study include any history of neurodevelopmental disease (e.g. autism, intellectual disability) or the presence of any previously reported symptomatic head injury. Given the low rate of recruitment for concussed athletes, none were excluded from participating in the current study.

Method

All participants completed two conditioning tasks, one aversive and one pleasant. All participants provided saliva samples to test for cortisol levels at two time points during the study (approximately 50-60 minutes apart). For the concussed athletes only, the details, symptoms and illness perceptions of the current injury were assessed.

Questionnaires

All questionnaires are summarized in Table 1, and described in detail below.

Intake Interview: The intake interview included questions addressing demographics, education, medical and psychiatric history, and life-long involvement in athletics. It also included questions regarding medications, caffeine, drug and alcohol use, and hours of sleep in the last 24 hours. As part of the psychiatric history section of the interview, participants were asked about any current suicidal ideation. No participants endorsed current suicidal ideation.

Brain Injury Symptom Questionnaire – Adapted (BISQ-A; Gordon et al., 2000): The BISQ-A was used to elicit any potential incidents in the participants' pasts that may have resulted in a traumatic brain injury or head injury. It includes questions about a variety of situations in which a brain injury may have occurred (i.e., while

snowboarding, while assaulted, while diving into water, etc.) as well as a number of situations that may have resulted in an emergency room visit or hospital stay (i.e., high fever, seizures, concussion, etc.). For any positive answer, the participant was asked to provide information about associated loss of consciousness and posttraumatic amnesia. The use of this questionnaire allows for a more nuanced history of brain injury exposure. Control participants who endorsed any previous head injuries with associated loss of consciousness were excluded from the present study.

Post-Concussion Symptom Scale (PCSS; Lovell et al., 2000): The PCSS is a subtest of the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) that assesses 22 current health symptoms that are commonly reported following a concussion. Each item is rated on a 7-point Likert scale ranging from 0 (Not experiencing), 1-2 (Minor), 3-4 (Moderate), to 5-6 (Severe). PCSS symptoms are divided into three categories: somatic ("Headache," "Fatigue,"etc.), cognitive ("Difficulty concentrating," "Difficulty remembering," etc.), and affective ("Irritability," "Feeling more emotional," etc.). Each participant receives a total score by summing all 22 items. Higher scores are associated with a higher severity of symptoms. The PCSS has demonstrated adequate psychometric properties, with high internal consistency reliability ($\alpha = .93$) across healthy high school and college students (Lovell et al., 2000) and validity demonstrated by significant difference in scores between recently concussed and non-concussed high school students (Schatz, Pardini, Lovell, Collins, & Podell, 2006).

Table 1.

Questionnaires

Variable	Measure	Subscales/Number of Items
Demographics/History	Intake Interview	Six Sections: Demographics; Education; Current Concussion; Medical/Psychiatric; Athletic History; Physiological Status
History of Concussion	BISQ -A	27
Coping	Brief COPE	Problem-focused/Approach (11); Social /Help-seeking (4); Avoidant/Dysfunctional (9)
Illness Representations	IPQ-R	Identity (18); Beliefs (38); Causes (19)
Outcome	PCSS	22
Outcome	DASS	Depression (14); Anxiety (14); Stress (14)

Depression Anxiety and Stress Scale (DASS; Lovibond & Lovibond, 1995): The DASS is a 42-item scale that measures symptoms of depression, anxiety, and stress. Each statement is rated on a 4-point Likert scale ranging from 0 ("Did not apply to me at all") to 3 ("Applied to me very much, or most of the time"). Three subscale scores (depression, anxiety, and stress) are generated by summing the relevant items comprising each subscale; each is categorized as normal, mild, moderate, severe, or extremely severe. Validity support for the DASS comes from its correlations with the BDI, BAI, and STAI in a clinical population (Henry & Crawford, 2005). It also exhibits high internal consistency across these three subscales (depression, α=.91; anxiety, α=.84; stress, α=.90, and factor analysis supports a 3-factor solution with between factor correlations ranging from .28 to .53 (Antony, Beliing, Cox, Enns, & Swimson, 1998). This 3-factor structure is also supported in TBI populations (Wong, Dahm, & Ponsford, 2013). It has been employed in research in both clinical and non-clinical populations (Antony et al., 1998; Henry & Crawford, 2005), as well as TBI populations (de Sousa et al., 2012; Wong, et al., 2013).

Brief COPE (Carver, 1997): The Brief COPE is a 28-item scale with response options ranging from 0 (I haven't been doing this at all) to 3 (I've been doing this a lot). The 28 items consist of 14 item pairs corresponding to: active coping, planning, positive reframing, acceptance, humour, religion, using emotional support, using instrumental support, self-distraction, denial, venting, substance use, behavioural disengagement, and self-blame (Carver, 1997). Factor analysis of this measure in mTBI populations supports a three factor structure – approach coping, avoidant coping, and social coping (Snell, Siegert, Hay-Smith, & Surgenor, 2011b). These three factors have demonstrated adequate internal consistency (approach, α=.80; avoidant, α=.77; social, α=.84) in this population (Snell et al., 2011b). It has been used in a

number of recent studies examining outcome following concussion (e.g. Covassin et al., 2013; Kontos, Elbin, Newcomer, Covassin, & Collins 2013).

The Illness Perception Questionnaire - Revised (IPQ-R; Weinman et al., 1996) assesses three aspects of illness perception: identity, beliefs, and causal attributions. It has been employed in various illness populations, including heart disease, rheumatoid arthritis, cancer, and diabetes (Moss-Morris, Weinman, Petrie, Horne, Cameron, & Buick, 2002). This measure has demonstrated adequate psychometric properties, including test-retest reliability (correlations ranging from .46 to .88) and discriminant validity as evidenced by its small to moderate associations with measures of negative and positive trait affect (Moss-Morris et al., 2002) It was revised by Snell and colleagues (2011a) for use in concussed populations by adding four concussion-specific items to the Identity Scale - memory problems, concentration problems, irritability, balance problems, as well as by changing the word "illness" to "head injury" throughout the questionnaire.

Physiological Measures

Participants were connected to the PowerLab data acquisition (DAQ) system to measure heart rate and skin conductance. The PowerLab device is an AD Instruments product used in a variety of research applications including human physiology. To measure heart rate, electrocardiography (ECG), which is the recording of electrical activity of the heart, was used. Three electrodes were attached to the surface of the skin, two on either side of the heart and one below the ribs. To measure skin conductance, bipolar finger electrodes were connected to the palmar surfaces of the pointer and ring finger of the participant's non-dominant hand. The data acquired through the PowerLab DAQ were analyzed by the accompanying LabChart software;

heart rate was analyzed as beats per minute (BPM) and skin conductance was analyzed in microsiemens (µs).

Aversive Conditioning Task

Stimuli: The stimuli for the aversive conditioning procedure consisted of six squares (black outline on white background) differing only in size gradient. For half of the participants (Group A, counterbalanced), the smallest of the squares served as the conditioned stimulus occasionally paired with an aversive sound (CS+), and the largest of the squares served as the neutral conditioned stimulus never paired with an aversive sound (CS-). For the other half of participants (Group B, counterbalanced) this was reversed (i.e., smallest square was the CS- and largest square was the CS+). This difference in presentation was quasi-randomized across participants to ensure equal group sizes. The remaining four squares of intermediate size served as generalization stimuli 1-4 (GS1, GS2, GS3, and GS4). The visual stimuli created for this task were adapted from other studies using shapes of different sizes for fear acquisition and generalization (Neumann, Waters, Westbury, & Henry, 2008; Lissek et al., 2010). The aversive sound served as the unconditioned stimulus (US); this sound consisted of a three-second recording of a three-pronged garden fork scraped over slate presented through a set of headphones and not exceeding an intensity of 82dB (A); this intensity was set by measuring the intensity of the sound through a set of headphones and finding the volume on the computer that was closest to this threshold without surpassing it. The use of this sound for aversive conditioning applications in collegiate populations and vulnerable populations has been supported (Neumann & Waters, 2006; Neumann et al., 2008). The wav file used for the US was the same wav file used in the Neumann et al. (2008) study.

Presented under each visual stimulus (i.e., CS+, CS-, GS1-4) was an 11-point Likert scale with three anchors: “Certain sound will not occur” at the left-most point, “Uncertain” at the middle point, and “Certain sound will occur” at the right-most point. During each presented stimulus, the participant was asked to indicate their expectation of the sound occurring following the presentation of the shape, according to this 11-point scale.

Procedure: The procedure was divided into four separate phases: 1) pre-acquisition, 2) acquisition, 3) generalization, and 4) extinction. Following each phase, the participant was asked to provide subjective ratings of each stimulus. Images of each stimulus and three 9-point Likert scales to measure the following dimensions: pleasantness (0 = very unpleasant, 8 = very pleasant), arousal (0 = very calm, 8 = very arousing), and interest (0 = very boring, 8 = very interesting), were presented one at a time on the computer screen.

1) *Pre-acquisition:* The CS+ and CS- were each presented twice, in a randomized order. Each presentation lasted eight seconds. There was a five second delay between presentations; during this time the screen was black. There was no sound during this phase.
2) *Acquisition:* The CS+ and CS- were each presented six times, in a randomized order. Each presentation lasted eight seconds. During CS- trials, the presentation of the stimulus was followed by five seconds of a black screen and no sound. During CS+ trials, the offset of the CS+ coincided with the onset of the US, which lasted three seconds. During the US, the screen was black. The presentation of the US was followed by two seconds of no sound and a black screen. The thirteen-second trial latency is based on research finding a thirteen-second skin conductance response following an eight-second CS (Neumann et al., 2008).

3) *Generalization*: The CS+, CS-, GS1, GS2, GS3, and GS4 were presented three times each, for a period of eight seconds each. During CS+ trials, the offset of the CS+ coincided with the onset of the US, which lasted three seconds. During the US, the screen was black. The presentation of the US was followed by two seconds of no sound and a black screen. The CS+ trials continued to include the US during this phase such that extinction did not occur. During CS- and GS1-4 trials, the presentation of the stimulus was followed by five seconds of a black screen and no sound.

4) *Extinction:* The CS+ and CS- were each presented four times, in a randomized order. Each presentation lasted eight seconds. There was a five second delay between presentations; during this time the screen was black. There was no sound during this phase.

Instructions: The following instructions were verbalized to participants at the beginning of this procedure: "You will now view some shapes on this screen. After some of the shapes, you will hear an unusual sound through these headphones. For each shape that you see, please indicate at the bottom of the screen whether you are certain the sound will not occur, are certain the sound will occur, or are uncertain." The participant was then asked if they had any questions. If they did not, they were asked to put on the headphones and begin the task.

Pleasant Conditioning Task

The pleasant conditioning procedure was exactly the same as the aversive conditioning procedure, with changes made only to the stimuli used:

Stimuli: The stimuli for the pleasant conditioning procedure consisted of six triangles (black outline on white background) differing only in the number of lines drawn inside. For half of the participants (Group X, counterbalanced), the triangle with the least number of lines drawn

inside served as the conditioned stimulus occasionally paired with a pleasant sound (CS+), and the triangle with the most number of lines drawn inside served as the neutral conditioned stimulus never paired with a pleasant sound (CS-). For the other half of participants (Group Y, counterbalanced) this was reversed (i.e., triangle with the least number of lines drawn inside was the CS- and triangle with the most number of lines drawn inside was the CS+). This difference in presentation was randomized across participants. The remaining four triangles with increasing numbers of lines drawn inside served as generalization stimuli 1-4 (GS1, GS2, GS3, and GS4). A pleasant sound served as the unconditioned stimulus (US); this sound consisted of a baby laughing, and was taken from the International Affective Digital Sounds (IADS) dataset, which demonstrated in a sample of 100 participants that this sound was rated as highly pleasurable (Bradley & Lang, 2007).

Both the aversive and pleasant conditioning tasks were presented using the computer program DirectRT.

Procedure

Clinical Participants

Concussed athletes were recruited through the SRCC. The post-injury evaluation was conducted by a member of the SRCC, and included the intake interview, BISQ, ImPACT, PCSS, and DASS. For those athletes who consented to completing the research component, an appointment was made based on the athlete's availability. Difficulties contacting the athletes and their limited availability led to some lags in scheduling the research component, and led to variability in time since injury within the concussed athlete group. The research component was conducted in a different room and began with a consent process. The consent process included an introduction to the physiological equipment and a request to access their SRCC data (including

intake interview, BISQ, ImPACT, PCSS, and DASS). Athletes began by providing a saliva sample and completing the IPQ-R and Brief COPE. The heart rate electrodes and skin conductance electrodes were then attached by the researcher or a trained research assistant. The skin conductance electrode was attached to the participant's nondominant hand. The heart rate electrodes were placed by the participant on their left side (below their rib cage) and underneath their collarbone on both sides. Given the sensitivity of the physiological equipment, a Velcro strap was attached around the participant's hand as a reminder to keep movement to a minimum. The participant was then asked to sit still for a period of 10 minutes to record baseline data. Following this baseline period, the athlete completed the aversive and pleasant conditioning tasks, which were counterbalanced across participants. Finally, athletes provided a second saliva sample.

Control Participants

The control participants were recruited through the Psychology Participant Pool and were assigned course credit. The appointment began with the consent process, which included an introduction to the physiological equipment. The participant then provided a saliva sample and completed the intake interview. They then completed the BISQ, Brief COPE, PCSS, and DASS. Following this, they physiological equipment was attached by the researcher or a trained research assistant. All participants were hooked up to the heart rate electrodes and skin conductance electrodes. The skin conductance equipment was attached to the participant's nondominant hand. The heart rate electrodes were placed by the participant on their left side (below their rib cage) and underneath their collarbone on both sides. Given the sensitivity of the physiological equipment, a Velcro strap was attached around the participant's hand as a reminder to keep movement to a minimum. The participant was asked to sit still for a period of 10 minutes to

record baseline data. Following this baseline period, the participant completed the aversive and pleasant conditioning tasks, which were counterbalanced across participants. Finally, participants provided a second saliva sample. The entire protocol took approximately 60 minutes in the concussed athlete group, and 90 minutes in the control group.

CHAPTER 4

RESULTS

Data Manipulation

Autonomic responses were calculated as follows:

Heart rate response: The mean heart rate during the 2 seconds prior to stimulus presentation was subtracted from the mean heart rate during the first 3 seconds of the stimulus presentation to reflect heart rate response. A negative value would thus reflect a decrease in heart rate from baseline to stimulus presentation, a value of 0 would reflect no change, and a positive value would reflect an increase in heart rate from baseline to stimulus presentation.

Skin conductance response: The difference between the trough and peak of the skin conductance values during the first 3 seconds following stimulus presentation were calculated to reflect skin conductance response, with a higher value reflecting a greater skin conductance response.

Cortisol: Cortisol levels were measured at two time points, approximately 50-60 minutes apart. Cortisol level at time two was subtracted from cortisol level at time one to reflect change in cortisol levels over time.

All other measures were manipulated as follows:

Reaction time: Reaction time was measured by the DirectRT program as the time from stimulus onset to when the participant made a response.

Expectancy ratings: Expectancy of the US was scored as a deflection from the middle "Uncertain" rating during the presentation of the CS+. The deflections were scored as a percentage change from the uncertain baseline. As a result, -100% indicated no expectancy (certain that the sound will NOT follow the stimulus), 0% indicated an uncertain expectation, and +100% indicated expectation of the US (certain that the sound WILL follow the stimulus). In both the aversive and pleasant conditioning tasks, expectancy ratings of the CS+ were averaged for each phase: pre-acquisition, acquisition, generalization, extinction. Number of trials to reach 100% expectancy and -100% expectancy in the acquisition and extinction trials, respectively, were also calculated. In participants who did not reach either 100% or -100% expectancy, this score was calculated as number of trials + 1.

A generalization quotient was created for each participant based on their expectancy ratings of generalization stimuli. The generalization quotient was calculated as follows: All expectancy ratings were summed for each generalization stimulus and then weighted based on their similarity to the CS+: the sum of GS1 (furthest from the CS+ in terms of size) expectancy ratings were multiplied by 4, the sum of GS2 multiplied by 3, the sum of GS3 multiplied by 2, and the sum of GS4 (closest to the CS+ in terms of size) multiplied by 1. All of these were then divided by 10 for a total generalization quotient (possible range -100 to +100), with -100 indicating no generalization and +100 indicating full generalization.

Questionnaires: For the PCSS, the total raw score was used as a measure of symptoms. The DASS-Anxiety subscale raw score was used as a measure of anxiety symptomatology. The subscale raw scores of the IPQ-R were used as measures of cognitive and emotional illness representations; these included: timeline (acute/chronic), timeline (cyclical), consequences, personal control, treatment control, illness coherence, and emotional representations. In terms of

the Brief COPE, based on the study by Snell et al. (2011b), items on this measure were divided into three coping dimensions: problem-focused/approach coping, avoidant coping, and social coping.

Participants

Control Group

Data were collected from 41 control participants. In order to select an appropriate control group that demonstrated some homogeneity, a number of steps were taken. A regression was conducted with major variables of interest to identify multivariate outliers using Mahalanobis distance. Using a critical value of 30.14, 2 participants were excluded. On baseline measures of the DASS, no athletes scored higher than in the normal or mild range of symptoms on any of the Depression, Anxiety, or Stress subscales. On the intake interview, no athletes endorsed either a past or present problem with anxiety or depression. Thus, all controls who scored in the moderate or higher range on the DASS on any subscale (n=4) or endorsed a present or past problem with anxiety or depression (n=11) were excluded. After these individuals were removed, all males were included in an effort to resemble the high male:female ratio in the concussed athlete group as closely as possible. Of the remaining females, those who had missing physiological data due to technical difficulties were removed (n=4). Given that the concussed group in this study consisted of varsity athletes, and that none of the control group participants were varsity athletes, physical activity levels were not comparable between the two groups. However, to create a control group that was somewhat homogenous in terms of physical activity, those participants who endorsed engaging in physical activity fewer than two times per week were removed (n=4); this resulted in the removal of the most sedentary participants within this group. Overall, these steps led to the selection of a final group of 15 control participants.

Concussed Athlete Group

Data were collected from 16 athletes. A regression was conducted with major variables of interest to identify multivariate outliers using Mahalanobis distance. Using a critical value of 30.14, 1 participant was excluded.

Characteristics of the two groups in terms of concussion history, past and current depression and anxiety, current stress level, level and description of physical activity, and male:female ratio are presented in Table 2.

Independent sample t-tests were used to compare the concussed athletes for whom baseline data from the beginning of the season were available (n = 12) to the control group on the DASS subscales of Depression, Anxiety, and Stress. As shown in Table 3, there were no differences between the groups on the Depression or Anxiety subscale, but the control participants endorsed higher levels of stress despite both groups being within the normal to mild range. Given the already small sample size, availability of baseline data for only some athletes, and technical difficulties leading to missing heart rate and skin conductance data for a number of participants (n = 9; 6 concussed athletes, 3 controls), these differences were not controlled for within the current study. Possible implications of these baseline differences are discussed in later sections.

Descriptives

The overall group of participants included 15 athletes (12 males, 3 females) and 15 controls (9 males, 6 females) with an average age of 19.70 years (*SD* = 1.47) and an average of 1.66 years (*SD* = 1.29) of post-secondary education. Athletes were seen anywhere between 3 and 52 days post-injury (*M* = 12.93, *SD* = 11.94), and their scores on the PCSS post-injury ranged from 0 to 71. Independent sample *t*-tests revealed that the PCSS scores were higher in the

Table 2.

Comparison of Concussed Athlete and Control Participant Groups

	Concussed Athletes	Control Participants
Previous concussions	Yes; Range from 0-4	No
Past depression/anxiety	None reported	None reported
DASS - Depression	Normal – mild range	Normal - mild range
DASS – Anxiety	Normal - mild range	Normal - mild range
DASS – Stress	Normal - mild range	Normal - mild range
Varsity Athlete	Yes	No
Physical Activity	Type of sport played included: hockey, basketball, football, volleyball, soccer, track-and-field	Amount of physical activity ranged from 2 times per week to daily; included cardiovascular activities, strength training, and yoga
Male: Female ratio	4:1	3:2

concussed athlete group (M = 25.87; SD = 26.12) than in the control group (M = 7.53; SD = 8.76), $t(17.11) = 2.58$, $p = .019$. Athletes' scores on the DASS-Anxiety subscale post-injury ranged from 0 to 17. There were no differences in anxiety symptoms between the concussed athlete group (M = 4.33; SD = 5.05) and the control group (M = 3.07; SD = 2.25), $t(19.35) = .89$, $p = .386$.

Table 3.

Baseline Measures of Depression, Anxiety, and Stress

	Concussed Athletes at Baseline		Control Group		t	Cohen's d
	M	SD	M	SD		
Depression	1.50	3.34	1.67	2.32	.15	.06
Anxiety	1.58	2.06	3.07	2.25	1.78	.69
Stress	1.67	2.35	7.53	4.66	4.25**	1.59

Note. ** p< .01

Statistical Analyses

All statistical analyses were conducted using IBM SPSS version 22.

Data Cleaning and Testing Assumptions

Each of the analyses included an initial check of the data for univariate outliers, with a z-score of ±3.00 serving as a cut-off. Checking assumptions for ANOVAs included checking for normality and homogeneity of variance. The assumption of normality was tested using the Shapiro-Wilk test; given the robustness of ANOVA to violations of normality, nonparametric tests or data transformations were only applied when tests of homogeneity of variance were also violated. The assumption of homogeneity of variance was tested using Levene's test. For repeated measures ANOVAs the assumption of sphericity was also checked using Mauchly's

Test of Sphericity; in cases of violation, a Greenhouse-Geisser correction was applied. Violations of these assumptions, as well as the corrective measures applied, are described within each of the analyses below.

Affective Outcomes following Concussion

Within the subset of athletes for whom baseline data were available (n = 12), possible changes from pre- to post-injury were examined on the DASS and PCSS. Four one-way within subjects ANOVAs were conducted to examine the effect of time point (baseline, post-injury) on DASS-Depression, DASS-Anxiety, DASS-Stress, and PCSS scores. These analyses revealed that, at the post-injury time point, athletes had higher PCSS scores, a trend towards higher DASS-Anxiety and DASS-Stress scores, and no difference in DASS-Depression scores. These findings are summarized in Table 4.

Table 4.

Changes in DASS and PCSS Scores from Baseline to Post-Injury in the Concussed Athlete Group

	Baseline	Post-Injury	*F*-value	*p*-value	Eta
DASS-D	1.50 (3.34)	3.58 (5.21)	2.72	.128	.20
DASS-A	1.58 (2.07)	4.00 (5.29)	3.76	.078	.26
DASS-S	1.67 (2.35)	6.42 (7.33)	4.39	.060	.29
PCSS	2.50 (3.63)	24.33 (27.21)	7.62	.019	.41

Note. Baseline and Post-Injury values reported as mean (standard deviation). D= Depression; A = Anxiety; S = Stress; PCSS = Post-Concussion Symptom Scale

Pre-Acquisition Trial

Concussed athletes and control participants were compared during the pre-acquisition phase to examine any possible differences in expectancy ratings, autonomic response (heart rate, skin conductance), or reaction time to the conditioned stimuli prior to their association with the

unconditioned stimuli in later task phases. As demonstrated in Table 5, there were no differences between the two groups on any of these measures.

Table 5.

Comparisons of Expectancy Ratings, Autonomic Response, and Reaction Time during the Pre-Acquisition Trial

	Concussed Athletes		Controls		T
	M	SD	M	SD	
Expectancy Ratings					
Aversive task	-24.67	36.03	-37.33	37.31	.946
Pleasant task	-20.71	39.90	-28.67	27.22	.631
HR Response					
Aversive task	2.37	6.04	4.64	7.45	-.761
Pleasant task	4.31	6.45	1.35	13.26	.639
SC Response					
Aversive task	1.07	1.01	.89	.70	.456
Pleasant task	1.05	1.18	.53	.33	1.397
Reaction Time					
Aversive task	3327.17	1600.97	3933.13	1384.70	-1.109
Pleasant task	3430.64	1389.27	3794.23	1227.97	-.748

Note. HR = Heart Rate; SC = Skin Conductance

Affective Ratings

In addition to testing possible differences between concussed athletes and control participants during the pre-acquisition phase, possible differences between the two groups in their affective ratings (pleasantness, interest, arousal) of the conditioned stimuli were examined

in both the aversive and pleasant conditioning tasks. This was completed to ensure that any differences between the two groups could be attributed to associative learning independent of any evaluative learning.

Aversive Task

To examine whether concussed athletes and control participants differed in their ratings of the stimuli, three one-way ANOVAs were conducted. A check of the data revealed absence of univariate outliers, and the presence of normality and homogeneity of variance. There were no differences between concussed athletes and controls in terms of their ratings of pleasantness, arousal, or interest of the CS+, $p > .05$ (see Table 6).

Table 6.

Affective Ratings of the Conditioned Stimulus during the Aversive Conditioning Task

	Control	Athlete	*F*-value	*p*-value	Eta
Interest	4.02 (1.48)	3.33 (1.63)	1.44	.240	.05
Arousal	3.62 (1.58)	4.13 (1.97)	.63	.435	.02
Pleasantness	3.00 (1.08)	3.10 (1.68)	.04	.847	.00

Note. Values reported as mean (standard deviation)

Pleasant Task

To examine whether concussed athletes and control participants differed in their ratings of the stimuli in the pleasant task, three one-way ANOVAs were conducted. A check of the data revealed absence of univariate outliers, and the presence of normality (with the exception of pleasant arousal ratings) and homogeneity of variance. Concussed athletes and controls did not differ in terms of their ratings of pleasantness, arousal, or interest of the CS+, $p > .05$ (see Table 7).

Table 7.

Affective Ratings of the Conditioned Stimulus during the Pleasant Conditioning Task

	Control	Athlete	*F*-value	*p*-value	Eta
Interest	4.62 (2.01)	3.33 (2.08)	2.88	.101	.10
Arousal	3.60 (1.73)	2.98 (1.97)	.81	.376	.03
Pleasantness	4.34 (1.80)	4.36 (2.15)	.00	.990	.00

Note. Values reported as mean (standard deviation)

Overall, these results indicate that concussed athletes and control participants were matched on measures of evaluative learning, including ratings of interest, arousal, and pleasantness in both aversive and pleasant conditioning tasks.

Hypothesis 1

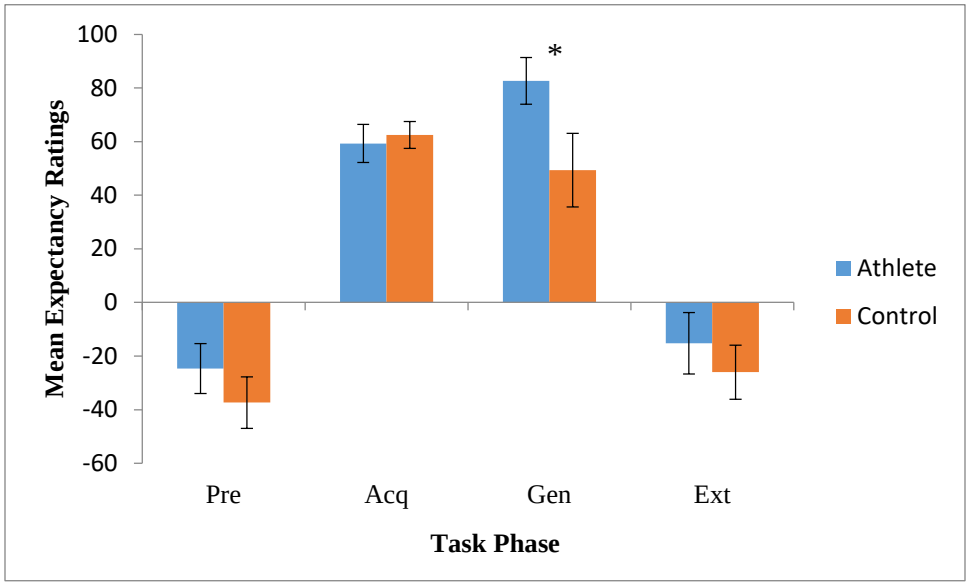
Aversive Task

To test the hypothesis that concussed athletes and controls differed in their average expectancy ratings of the CS+, a two (group: concussed athlete, control) by three (phase: acquisition, generalization, extinction) mixed factorial ANOVA was conducted on average expectancy ratings. The data were analysed for univariate outliers and one participant was identified and removed. The Shapiro-Wilk test and Levene's test demonstrated normality and homogeneity of variance across all phases, with the exception of the generalization phase. As expected, there was a main effect of phase on expectancy ratings, $F(2, 54) = 53.94$, $p = .000$, $\eta_p^2 = .67$, indicating that expectancy ratings differed across the three phases of the task. The pattern of results showed that participants were more expectant of the aversive sound following the CS+ during the acquisition and generalization phases, and less expectant during the extinction phase (see Figure 1). There was no main effect of group, $F(1, 27) = 2.31$, $p = .140$,

η_p^2 = .08. There was no interaction of group and phase, $F(2, 54) = 2.00$, p = .145, η_p^2 = .07. Expectancy ratings across the four phases by group are demonstrated in Figure 1. To test the hypothesis that concussed athletes would learn the association faster in the acquisition phase and extinguish the association more slowly in the extinction trial, two one-way ANOVAs were conducted. There were no differences in the number of trials it took to reach 100% expectancy in the acquisition phase of the aversive task between concussed athletes (M = 3.13, SD = 1.41) and healthy controls (M = 3.20, SD = 1.52), $F(1,28) = .02$, p = .902, η_p^2 = .00. There were similarly no differences in the number of trials it took to reach -100% expectancy in the extinction phase of the aversive task between concussed athletes (M = 3.60, SD = 1.40) and healthy controls (M =3.47 , SD = 1.30), $F(1,28) = .07$, p = .789, η_p^2 = .00.

Figure 1.

Mean Expectancy Ratings across Phases of the Aversive Conditioning Task



Note. Error bars represent the standard error

To test the hypothesis that concussed athletes and controls differed in their generalization of the conditioned stimulus to similar stimuli, a one-way ANOVA was conducted on

generalization quotients. This analysis demonstrated that controls (M = -37.82, SD = 27.70) and concussed athletes (M = -43.60, SD = 43.12) were not different in their generalization of the conditioned stimulus, $F(1,28) = .19$, p = .666, $\eta_p^2 = 01$.

Pleasant Task

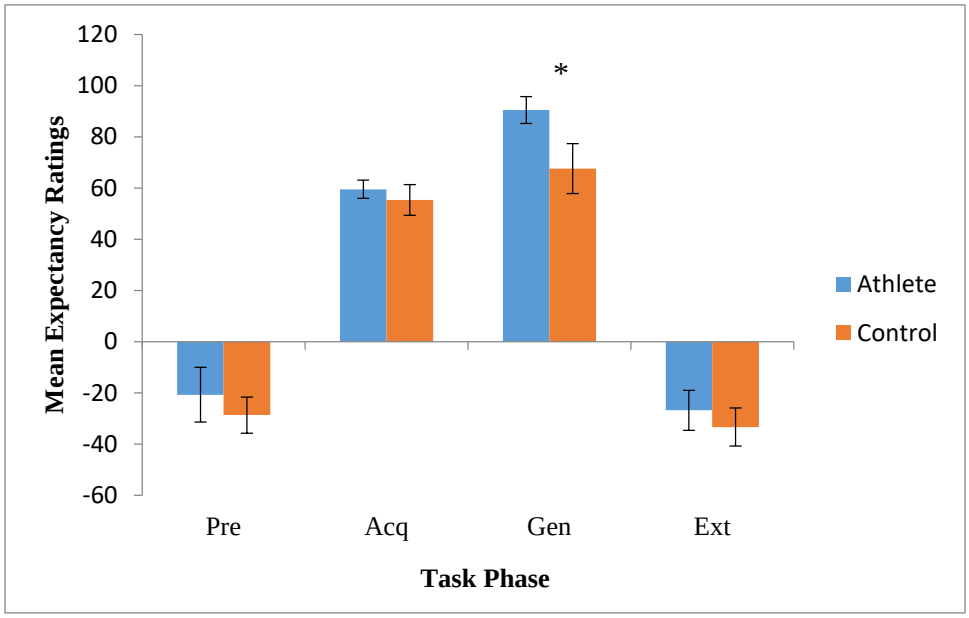
To explore whether concussed athletes and controls differed in their average expectancy ratings of the CS+, a two (group: concussed athlete, control) by three (phase: acquisition, generalization, extinction) mixed factorial ANOVA was conducted on average expectancy ratings. Analysis of the data did not reveal the presence of any univariate outliers; however, due to technical errors, one participant's data was not available for analysis. The Shapiro-Wilk test revealed non-normality of data across all phases. Levene's test of homogeneity of variance was significant for the generalization phase, and thus the Mann-Whitney U Test for nonparametric data was used for post-hoc analyses of expectancy ratings during the generalization phase. Using a Greenhouse-Geisser correction for sphericity, there was a main effect of phase on expectancy ratings, $F(1.75, 47.21) = 122.68$, p = .000, $\eta_p^2 = .82$. The pattern of results showed that participants were more expectant of the pleasant sound following the CS+ during the acquisition and generalization phases, and less expectant during the extinction phase (see Figure 2). There was a main effect of group, indicating that ratings from concussed athletes and controls were different, $F(1, 27) = 6.15$, p = .020, $\eta_p^2 = .19$. There was no interaction of group and phase, $F(1.75, 47.21) = 1.82$, p = .178, $\eta_p^2 = .06$. To explore whether or not athletes differed from controls in the number of trials to reach acquisition and extinction, two one-way ANOVAs were conducted. There were no differences in the number of trials it took to reach 100% expectancy in the acquisition phase of the pleasant task between concussed athletes (M = 3.14, SD = 1.29) and healthy controls (M = 3.60, SD = 1.88), $F(1,27) = .57$, p = .456, $\eta_p^2 = .02$. There were similarly

no differences in the number of trials it took to reach -100% expectancy in the extinction phase of the pleasant task between concussed athletes (M = 3.00, SD = .88) and healthy controls (M = 3.20, SD = 1.27), $F(1,27) = .24$, p = .627, $\eta_p^2 = .01$.

Post-hoc analyses: Possible differences between groups during the acquisition and extinction phases of the pleasant task were investigated using two one-way ANOVAs. There were no differences in expectancy ratings between athletes and controls during the acquisition phase, $F(1,28) = .35$, p = .202, or extinction phase, $F(1,28) = .37$, p = .548. Using the Mann-Whitney U Test, a difference was identified in expectancy ratings between concussed athletes and controls during the generalization phase, $p = .010$, with athletes having higher average expectancy ratings. Expectancy ratings of the CS+ by group across task phases are demonstrated in Figure 2.

Figure 2.

Mean Expectancy Ratings across Phases of the Pleasant Conditioning Task



Note. * = p< .05. Error bars represent the standard error

To explore whether or not concussed athletes and controls differed in their generalization of the conditioned stimulus to similar stimuli, a one-way ANOVA was conducted on generalization quotients. This analysis demonstrated that controls (M = -48.47, SD = 30.53) and athletes (M = -51.82, SD = 30.53) were not different, $F(1,28) = .091$, p = .77 $\eta_p^2 = .00$.

Exploratory analyses: Given the difference in expectancy ratings between concussed athletes and controls during the generalization phase of the pleasant task, an exploratory analysis was used to look for a possible similar trend in the aversive conditioning task. Given that tests of normality and homogeneity of variance were violated for expectancy ratings in this phase of the aversive task, a nonparametric test was used to examine these differences. The Mann-Whitney U Test indicated that there was a difference between athletes and controls in their expectancy ratings during the generalization phase of the aversive task, p = .016, with athletes having higher average expectancy ratings.

Given the unexpected finding that concussed athletes demonstrated higher expectancy ratings during the generalization phase, expectancy ratings across all presentations of the conditioned stimulus in all four phases were examined (see Figures 3 and 4). It was hypothesized that the higher ratings during the generalization phase may reflect differences in persistence of the conditioned response (i.e., expectancy) following the acquisition phase. Exploratory analyses were conducted to examine this hypothesis. Four one-way ANOVAs were conducted to examine possible differences in 1) the first presentation of the conditioned stimulus during the generalization phase of the aversive task, 2) the first presentation of the conditioned stimulus during the generalization phase of the pleasant task, 3) the first presentation of the conditioned stimulus during the extinction phase of the aversive task, and 4) the first presentation of the conditioned stimulus during the extinction phase of the pleasant task. During the generalization

phase of the aversive task, expectancy ratings for the first presentation of the conditioned stimulus were higher in the concussed athlete group (M = 69.33, SD = 51.75) than the healthy control group (M = 10.00, SD = 69.17), $F(1,27) = 6.90$, p = .014, $\eta_p^2 = .20$. Similarly, during the generalization phase of the pleasant task, expectancy ratings for the first presentation of the conditioned stimulus were higher in the concussed athlete group (M = 84.29, SD = 36.10) than the healthy control group (M = 36.00, SD = 65.99), $F(1,27) = 5.85$, p = .023, $\eta_p^2 = .18$. During the extinction phase of the aversive task, expectancy ratings for the first presentation of the conditioned stimulus were higher in the concussed athlete group (M = 76.00, SD = 54.09) than the healthy control group (M = 48.00, SD = 52.26), however these were not statistically significant, $F(1,27) = 2.08$, p = .160, $\eta_p^2 = .07$. During the extinction phase of the pleasant task, expectancy ratings for the first presentation of the conditioned stimulus were higher in the concussed athlete group (M = 100.00, SD = .00) than the healthy control group (M = 54.67, SD = 41.03), $F(1,27) = 17.05$, p = .000, $\eta_p^2 = .39$.

Given the variability in time since injury in the concussed athlete group, possible correlations between days since injury and expectancy ratings were examined. As shown in Table 8, there were no correlations between days of injury and expectancy ratings to the conditioned stimuli in the acquisition, generalization, or extinction phases for either the aversive or pleasant task.

Overall, concussed athletes and controls did not differ in their expectancy ratings of the conditioned stimulus during the acquisition or extinction phases. They did, however, differ in their expectancy ratings of the conditioned stimulus during the generalization phase. Concussed athletes and controls did not differ in the number of trials it took to reach acquisition or extinction. There were similarly no differences in their generalization quotients. This pattern of

Figure 3.

Mean Expectancy Ratings to the Conditioned Stimulus by Presentation across all Phases of the Aversive Task

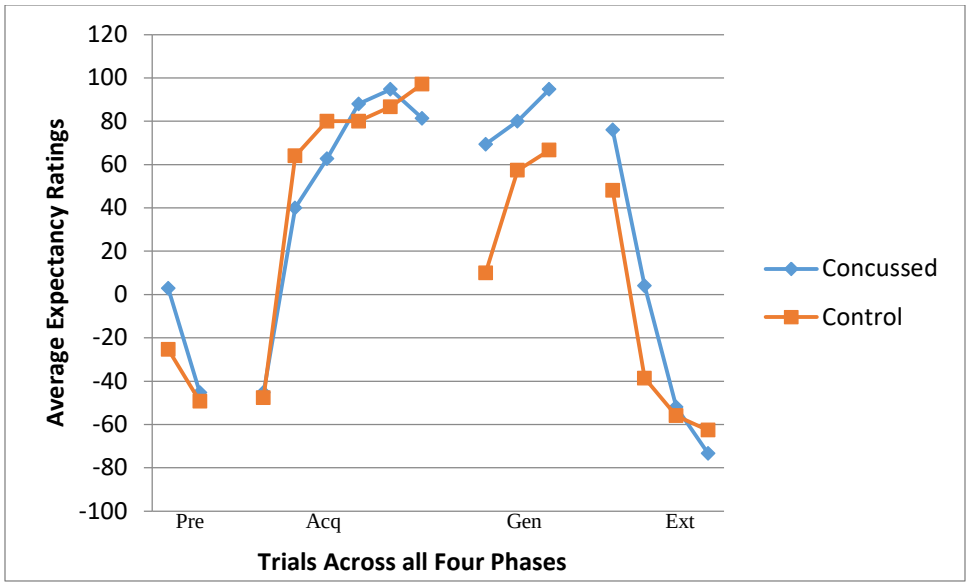
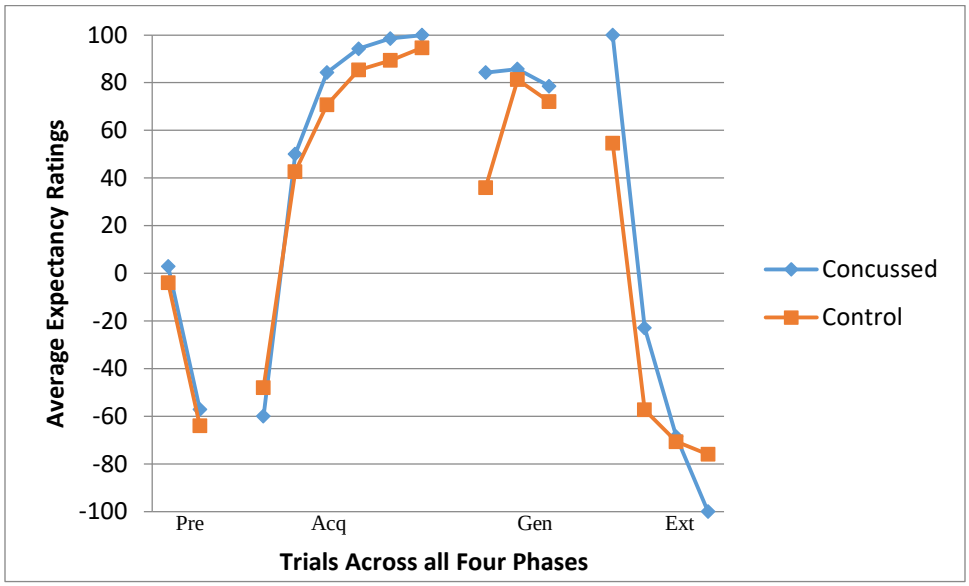


Figure 4.

Mean Expectancy Ratings to the Conditioned Stimulus by Presentation across all Phases of the Pleasant Task



results was observed in both the aversive and pleasant conditioning tasks. Exploratory analyses also indicated that concussed athletes demonstrated higher expectancy ratings of the conditioned stimulus during the first presentation in both the generalization and extinction phases, possibly indicating persistence of the classical conditioning effects in the absence of any differences in extinction. The hypothesis that concussed athletes and controls would differ in their learning of the association between the conditioned stimulus (CS+) and the unconditioned stimulus (US) was therefore only partially supported.

Table 8.

Correlations between Days since Injury and Mean Expectancy Ratings during the Acquisition, Generalization, and Extinction Phases of the Aversive and Pleasant Conditioning Tasks

	Acquisition	Generalization	Extinction
Aversive Task			
Days Since Injury	.01 (.967)	-.17 (.536)	-.38 (.167)
Pleasant Task			
Days Since Injury	-.06 (.834)	-.23 (.422)	-.34 (.232)

Note. Values reported as correlation coefficients (p values)

Hypothesis 2

Aversive Task

Heart Rate Response: To test the hypothesis that concussed athletes and controls differed in their heart rate response to the CS+, a two (group: concussed athlete, control) by three (phase: acquisition, generalization, extinction) mixed factorial ANOVA was conducted on average heart rate response. Data checking identified some non-normality in these data, but homogeneity of variance was not violated. No outliers were identified. There was no main effect of phase on heart rate response, $F(2, 38) = .26$, $p = .771$, $\eta_p^2 = .01$. There was no main effect of group, $F(1,$

19) = 1.28, p = .273, η_p^2 = .06. There was no interaction of group and phase, $F(2, 38)$ = .46, p = .636, η_p^2 = .02. One sample t-tests revealed that none of the mean heart rate responses for either the control group or concussed athlete group differed from 0 (p>.05), suggesting that there was no heart rate response, either increase or decrease, to the conditioned stimuli. Mean heart rate and heart response across phases are demonstrated in Table 9.

Table 9.

Mean Heart Rate (BPM) and Heart Rate Response during First Three Seconds of Conditioned Stimulus Presentation in the Aversive Task

		Pre-Acquisition	Acquisition	Generalization	Extinction
Control	HR	64.60 (18.45)	66.80 (13.90)	66.16 (15.07)	65.17 (18.12)
	HR Response	-4.64 (7.45)	-1.13 (3.37)	-.94 (9.15)	-2.82 (7.24)
Athlete	HR	58.26 (10.88)	62.73 (8.51)	64.41 (9.33)	63.35 (11.09)
	HR Response	-2.37 (6.04)	1.23 (4.95)	-.60 (4.35)	.62 (4.59)

Note. Values reported as mean (standard deviation). HR = Heart rate. Heart rate response calculated by subtracting mean heart rate in 2 seconds preceding stimulus onset from mean heart rate in 3 seconds following stimulus

To test the hypothesis that control participants and concussed athletes differed in their heart rate response to the generalization stimuli, a two (group: concussed athlete, control) by four (generalization stimulus: 1, 2, 3, 4) mixed factorial ANOVA was conducted. There was no main effect of stimulus, $F(3, 57)$ = .15, p = .930, η_p^2 = .01. There was no main effect of group, $F(1,19)$ = 2.70, p = .117, η_p^2 = .12. There was no interaction, $F(3, 57)$ = .68, p = .567, η_p^2 = .04.

Skin Conductance: To test the hypothesis that concussed athletes and controls differed in their average skin conductance response to the CS+, a two (group: concussed athlete, control) by three (phase: acquisition, generalization, extinction) mixed factorial ANOVA was conducted on

average skin conductance response. Data checking revealed no outliers, but did reveal significant non-normality in the data, as well as violations of homogeneity of variance. Data was thus transformed using a base-10 log prior to analysis. There was no main effect of phase on skin conductance response, $F(2, 38) = .36$, $p = .698$, $\eta_p^2 = .02$. There was no main effect of group, $F(1, 19) = .13$, $p = .720$, $\eta_p^2 = .01$. There was no interaction of group and phase, $F(2, 38) = .73$, $p = .490$, $\eta_p^2 = .04$. Mean skin conductance and skin conductance response across phases are displayed in Table 10.

Table 10.

*Mean Skin Conductance (*µs*) and Skin Conductance Response during First Three Seconds of Conditioned Stimulus Presentation in the Aversive Task*

		Pre-Acquisition	Acquisition	Generalization	Extinction
Control	SC	9.34 (6.62)	8.72 (5.74)	8.60 (5.22)	9.82 (5.17)
	SCR	.89 (.70)	.56 (.29)	.54 (.32)	.73 (.49)
Athlete	SC	9.38 (5.62)	10.01 (5.05)	11.04 (6.41)	11.60 (5.94)
	SCR	1.07 (1.01)	.68 (.62)	.95 (.88)	.92 (1.00)

Note. Values reported as mean (standard deviation). SC = Skin Conductance; SCR = Skin Conductance Response. Skin conductance response calculated by subtracting the trough value from the peak value during the first 3 seconds of stimulus presentation

To test the hypothesis that control participants and concussed athletes differed in their skin conductance response to the generalization stimuli, a two (group: concussed athlete, control) by four (generalization stimulus: 1, 2, 3, 4) mixed factorial ANOVA was conducted. There was no effect of stimulus, $F(3, 57) = .53$, $p = .662$, $\eta_p^2 = .03$. There was no effect of group, $F(1,19) = .05$, $p = .830$, $\eta_p^2 = .00$. There was also no interaction, $F(3, 57) = .24$, $p = .865$, $\eta_p^2 = .01$.

Pleasant Task

Heart Rate Response: To explore whether concussed athletes and controls differed in their average heart rate response to the CS+, a two (group: concussed athlete, control) by three (phase: acquisition, generalization, extinction) mixed factorial ANOVA was conducted on average heart rate response. Data checking identified some non-normality, but homogeneity of variance was not violated and no significant outliers were identified. Using a Greenhouse-Geisser correction, there was no main effect of phase on heart rate response, $F(1.52, 28.91) = .43$, $p = .599$, $\eta_p^2 = .02$. There was no effect of group, $F(1, 19) = 3.46$, $p = .078$, $\eta_p^2 = .15$. There was no interaction of group and phase, $F(1.52, 28.91) = 2.08$, $p = .153$, $\eta_p^2 = .10$. One sample t-tests revealed that none of the mean heart rate responses for either the control group or concussed athlete group differed from 0 ($p>.05$), suggesting that there was no heart rate response, either increase or decrease, to the conditioned stimuli. Mean heart rate and heart response across phases are demonstrated in Table 11.

Table 11.

Mean Heart Rate (BPM) and Heart Rate Response during First Three Seconds of Conditioned Stimulus Presentation in the Pleasant Task

		Pre-Acquisition	Acquisition	Generalization	Extinction
Control	HR	60.46 (17.88)	66.22 (14.68)	66.92 (17.39)	64.69 (17.59)
	HR Response	-1.35 (13.26)	-2.68 (5.39)	-.87 (4.08)	-4.99 (8.33)
Athlete	HR	61.97 (15.27)	63.52 (8.36)	64.86 (8.57)	63.96 (11.71)
	HR Response	-4.31 (6.45)	-.42 (3.40)	-.53 (3.29)	1.01 (4.10)

Note. Values reported as mean (standard deviation). HR = Heart rate. Heart rate response calculated by subtracting mean heart rate in 2 seconds preceding stimulus onset from mean heart rate in 3 seconds following stimulus onset

To explore whether control participants and concussed athletes differed in their heart rate response to the generalization stimuli, a two (group: concussed athlete, control) by four

(generalization stimulus: 1, 2, 3, 4) mixed factorial ANOVA was conducted. There was no effect of stimulus, $F(3, 54) = 1.01$, p = .394, $\eta_p^2 = .05$. There was no effect of group, $F(1,18) = 2.05$, p = .170, $\eta_p^2 = .10$. There was also no interaction, $F(3, 54) = .49$, p = .693, $\eta_p^2 = .03$.

Skin Conductance: To explore whether concussed athletes and controls differed in their average skin conductance response to the CS+, a two (group: concussed athlete, control) by three (phase: acquisition, generalization, extinction) mixed factorial ANOVA was conducted on average skin conductance response. Data checking revealed no outliers, but did reveal significant non-normality in the data, as well as violations of homogeneity of variance. Data was thus transformed using a base-10 log prior to analysis. There was no main effect of phase on skin conductance response, $F(2,38) = .95$, p = .395, $\eta_p^2 = .05$. There was no main effect of group, $F(1, 19) = .19$, p = .668, $\eta_p^2 = .01$. There was also no interaction of group and phase, $F(2, 38) = .23$, p = .797, $\eta_p^2 = .01$. Mean skin conductance and skin conductance response across phases are displayed in Table 12.

Table 12.

*Mean Skin Conductance (*µs*) and Skin Conductance Response during First Three Seconds of Conditioned Stimulus Presentation in the Pleasant Task*

		Pre-Acquisition	Acquisition	Generalization	Extinction
Control	SC	8.74 (5.84)	8.22 (5.11)	7.37 (4.15)	6.48 (4.25)
	SCR	.53 (.33)	.55 (.40)	.49 (.40)	.34 (.29)
Athlete	SC	9.83 (5.58)	9.72 (5.90)	9.95 (6.55)	10.81 (6.75)
	SCR	1.05 (1.18)	.60 (.47)	.58 (.56)	.53 (.44)

Note. Values reported as mean (standard deviation). SC = Skin Conductance; SCR = Skin Conductance Response. Skin conductance response calculated by subtracting the trough value from the peak value during the first 3 seconds of stimulus presentation

To explore whether control participants and concussed athletes differed in their skin conductance response to the generalization stimuli, a two (group: concussed athlete, control) by four (generalization stimulus: 1, 2, 3, 4) mixed factorial ANOVA was conducted. There was a main effect of stimulus, $F(3, 54) = 5.00$, $p = .004$, $\eta_p^2 = .22$. There was no main effect on group, $F(1,18) = .15$, $p = .708$, $\eta_p^2 = .01$. There was no interaction, $F(3, 57) = .57$, $p = .635$, $\eta_p^2 = .03$.

Given the variability in days since injury in the concussed athlete group, possible correlations between days since injury and autonomic responses were examined. As shown in Table 13, there were no correlations between days of injury and heart rate response to the conditioned stimuli in the acquisition, generalization, or extinction phases of either the aversive or pleasant task. Similarly, as shown in Table 14, there were no correlations between days of injury and skin conductance response to the conditioned stimuli in the acquisition, generalization, or extinction phases of either the aversive or pleasant task.

Table 13.

Correlations between Days since Injury and Heart Rate Response (BPM) across Acquisition, Generalization, and Extinction Phases of the Aversive and Pleasant Conditioning Tasks

	Acquisition	Generalization	Extinction
Aversive Task			
Days Since Injury	.34 (.343)	.33 (.349)	.03 (.925)
Pleasant Task			
Days Since Injury	.14 (.703)	.14 (.710)	.05 (.895)

Note. Values reported as correlation coefficients (p values). Heart rate response calculated by subtracting mean heart rate in 2 seconds preceding stimulus onset from mean heart rate in 3 seconds following stimulus onset

Table 14.

Correlations between Days since Injury and Skin Conductance Response (µs) across Acquisition, Generalization, and Extinction Phases of both the Aversive and Pleasant Conditioning Tasks

	Acquisition	Generalization	Extinction
Aversive Task			
Days Since Injury	-.41 (.237)	-.29 (.413)	-.48 (.159)
Pleasant Task			
Days Since Injury	.42 (.222)	.62 (.057)	-.17 (.646)

Note. Values reported as correlation coefficients (p values). Skin conductance response calculated by subtracting the trough from the peak value in the 3 seconds following stimulus onset

Overall, the hypothesis that control participants and concussed athletes would differ in their autonomic response to the conditioned stimulus (CS+) was not supported in the aversive conditioning task. There were also no differences between the two groups in autonomic response during the pleasant conditioning task.

Hypothesis 3

Cortisol samples were analyzed for a subset of the participants (n = 20). To test the hypothesis that concussed athletes would demonstrate a greater cortisol-related stress response, a two-way (group: concussed athlete, control) repeated measures (time 1, time 2) ANOVA was conducted on cortisol levels. One univariate outlier was removed from these analyses. There was a main effect of time, with higher cortisol levels at time 1 than at time 2, $F(1,17) = 7.93$, p = .012, $\eta_p^2 = .32$. There was no main effect of group, $F(1,17) = 2.22$, p = .155, $\eta_p^2 = .12$. There was no interaction of time and group, $F(1,17) = 1.29$, p = .272, $\eta_p^2 = .07$. Descriptives are shown in Table 15.

Table 15.

Mean Salivary Cortisol Levels (µg/dL) at Time 1, Time 2, and Change over Time

	Time 1	Time 2	Change
Control	.17(.13)	.13(.05)	.04(.10)
Athlete	.28(.17)	.18(.08)	.10(.12)

Note. Values reported as mean (standard deviation). Change calculated by subtracting salivary cortisol levels at Time 2 from salivary cortisol levels at Time 1. Time 2 was approximately 50-60 minutes following Time 1

Given the variability in days since injury in the concussed athlete group, possible correlations between days since injury and salivary cortisol levels were examined. As shown in Table 16, there were no correlations between days of injury and cortisol levels at time 1, time 2, or change in cortisol levels over time.

Table 16.

Correlations between Days since Injury and Salivary Cortisol Levels (µg/dL) at Time 1, Time 2, and Change over Time

	Time 1	Time 2	Change
Days Since Injury	-.45 (.197)	-.38 (.283)	-.40 (.252)

Note. Values reported as correlation coefficients (p values)

Overall, the hypothesis that concussed athletes would demonstrate a higher cortisol-related stress response (i.e., cortisol levels would decrease less over time) was not supported.

Hypothesis 4

Aversive Task

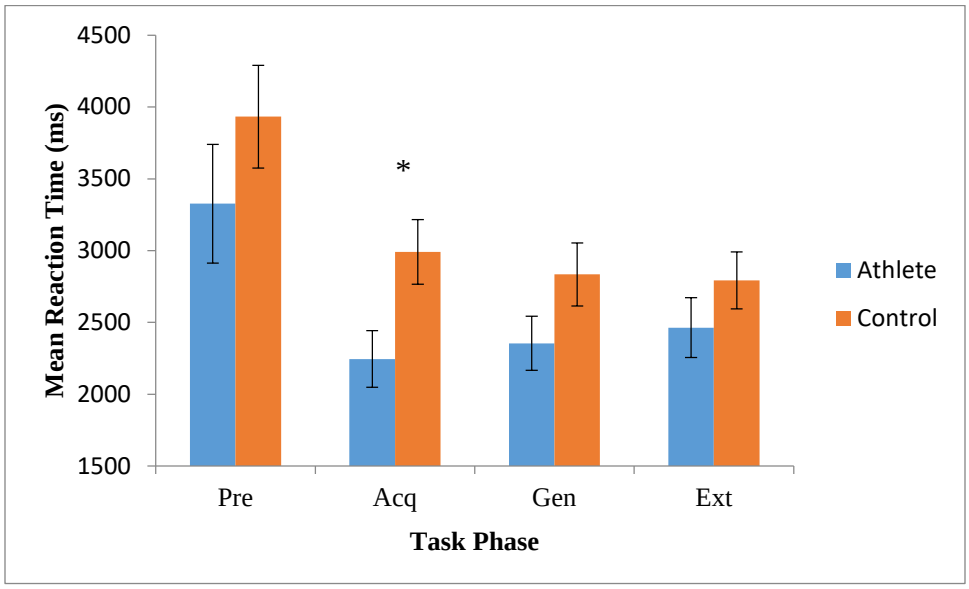
To test the hypothesis that concussed athletes and controls differed in their reaction time to the CS+, a two (group: concussed athlete, control) by three (phase: acquisition, generalization, extinction) mixed factorial ANOVA was conducted on average reaction time. No univariate

outliers were identified, and assumptions of normality and homogeneity of variance were met. There was no main effect of phase on reaction times, $F(2, 56) = .02$, $p = .980$, $\eta_p^2 = .00$. There was a main effect of group, $F(1, 28) = 6.08$, $p = .020$, $\eta_p^2 = .18$. There was no interaction of group and phase, $F(2, 56) = .72$, $p = .489$, $\eta_p^2 = .03$. Mean reaction time by group across phases is demonstrated in Figure 5.

Post-hoc analyses: To test possible group differences in each phase, three one-way ANOVAs were conducted. There was a difference during the acquisition phase, with athletes demonstrating faster reaction times to the CS+, $F(1,29) = 6.20$, $p = .019$. There were no differences during the generalization phase, $F(1,29) = 2.77$, $p = .107$, or the extinction phase, $F(1,29) = 1.32$, $p = .261$.

Figure 5.

Mean Reaction Times (ms) to the Conditioned Stimulus across all Phases of the Aversive Conditioning Task



Note. * = $p < .05$. Error bars represent the standard error

To test the hypothesis that concussed athletes and controls differed in their reaction time to the generalization stimuli, a one-way ANOVA was conducted. There were no differences

between the concussed athletes (M = 2498.46, SD = 716.99) and controls (M = 2862.81, SD = 570.50) in average reaction time to the generalization stimuli, $F(1,28) = 2.37$, p = .135, $\eta_p^2 = .08$.

Pleasant Task

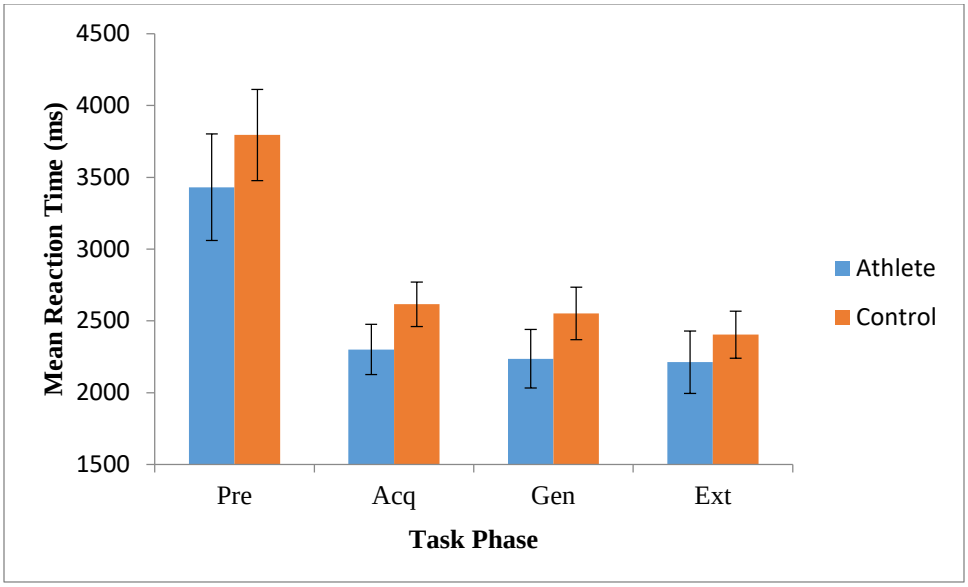
To explore whether concussed athletes and controls differed in their reaction time to the CS+, a two (group: concussed athlete, control) by three (phase: acquisition, generalization, extinction) mixed factorial ANOVA was conducted on average reaction time. No univariate outliers were identified, but one participant was removed due to technical errors and missing data. The distribution of reaction time data was found to be normal, with the exception of during the generalization phase, and the assumption of homogeneity of variance was met across phases. There was no main effect of phase on reaction times, $F(2, 54) = .75$, p = .477, $\eta_p^2 = .03$. There was no main effect of group, $F(1, 27) = 1.60$, p = .217, $\eta_p^2 = .06$. There was no interaction of group and phase, $F(2, 54) = .17$, p = .846, $\eta_p^2 = .01$. Reaction times by group across phases are presented in Figure 6.

To explore whether concussed athletes and controls differed in their reaction time to the generalization stimuli, a one-way ANOVA was conducted. There were differences between the concussed athletes (M =2492.28, SD = 355.95) and controls (M = 2925.70, SD = 651.66) in average reaction time to the generalization stimuli, $F(1,27) = 4.84$, p = .037, $\eta_p^2 = .15$, with athletes responding faster.

Given the variability in days since injury in the concussed athlete group, possible correlations between days since injury and reaction times were examined. As shown in Table 17, there were no correlations between days of injury and reaction time to the conditioned stimuli in the acquisition, generalization, or extinction phases for either the aversive or pleasant task.

Figure 6.

Mean Reaction Times (ms) to the Conditioned Stimulus across all Phases of the Pleasant Conditioning Task



Note. Error bars represent the standard error

Table 17.

Correlations between Days since Injury and Reaction Time (ms) across Acquisition, Generalization, and Extinction Phases of both the Aversive and Pleasant Conditioning Tasks

	Acquisition	Generalization	Extinction
Aversive Task			
Days Since Injury	.39 (.149)	.05 (.859)	-.22 (.438)
Pleasant Task			
Days Since Injury	-.01 (.975)	-.19 (.513)	-.36 (.209)

Note. Values reported as correlation coefficients

Overall, the hypothesis that concussed athletes and controls would differ in their reaction time to the conditioned stimulus (CS+) was partially supported. Concussed athletes had faster reaction times during the acquisition phase in the aversive, but not pleasant, task. Contrary to expectations, there were no differences in reaction time during the generalization or extinction

phases. Concussed athletes demonstrated significantly faster reaction times to the generalization stimuli in the pleasant, but not aversive, task.

Hypothesis 5

Based on the Common Sense Model's framework in which coping is purported to mediate the relationship between illness representations and outcome, possible relationships between illness representations, coping, PCSS scores, and DASS-Anxiety scores in this group were examined. Correlations between the IPQ-R cognitive and emotional representation subscales and the PCSS and DASS-Anxiety subscale were analyzed to identify potential illness representations of interest in predicting outcome. As can be seen in Table 18, timeline-cyclical beliefs were positively correlated with both the PCSS and DASS-Anxiety. Individuals who scored highly on this subscale endorsed items such as "My symptoms come and go in cycles," and "My head injury is very unpredictable." Personal control was significantly correlated with PCSS scores, but not DASS-Anxiety scores. Individuals who scored highly on the personal control subscale endorsed items such as "There is a lot which I can do to control my symptoms," and "The course of my head injury depends on me."

Relationships between the subscales of the Brief COPE, PCSS, and DASS-Anxiety were also analyzed using bivariate correlations to identify possible coping styles of interest. As shown in Table 19, there was a significant correlation between problem-focused/approach coping and the PCSS, but not the DASS-Anxiety subscale. The problem-focused/approach coping subscale includes items such as "I've been taking action to try to make the situation better" and "I've been thinking hard about what steps to take." It also includes coping strategies using acceptance, humour, and religion.

Table 18.

Correlations between Illness Representations and Outcome Measures

	PCSS	DASS-Anxiety
Timeline-Acute/Chronic	.28	.45
Timeline-Cyclical	.61*	.68**
Personal Control	.59*	.31
Treatment Control	.17	-.04
Consequences	.33	.25
Illness Coherence	-.35	-.45
Emotional Representations	.42	.30

Note. * = $p < .05$, ** = $p < .01$. Values reported as correlation coefficients

Table 19.

Correlations between Coping Subscales and Outcome Measures

	Problem-focused/Approach	Social coping/Help - seeking	Avoidant/Dysfunctional
PCSS	.66**	.33	.40
DASS-Anxiety	.41	.20	.14

Note. ** = $p < .01$. Values reported as correlation coefficients

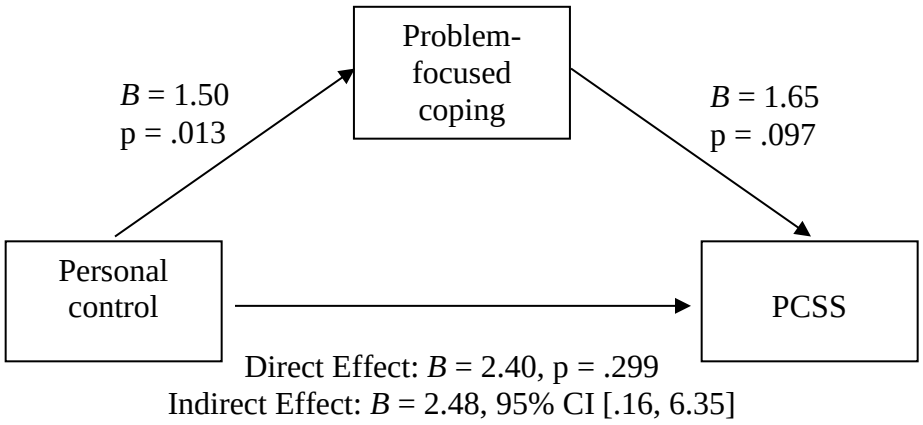
Given the relationship between the illness representations of timeline- cyclical and personal control with PCSS scores, as well as problem-focused coping and PCSS scores, possible mediation relationships were examined between these two illness representations and outcome (PCSS), with problem focused coping as a proposed mediator. These two mediational relationships were analyzed using the PROCESS model developed by Hayes (2013), who

suggests that this method has higher power than other mediation tests (e.g. Sobel test, causal steps approach), particularly in smaller sample sizes.

The relationship between personal control and symptoms on the PCSS was mediated by problem-focused coping. As Figure 7 illustrates, the standardized regression coefficient between personal control and problem-focused coping was statistically significant, while the standardized regression coefficient between problem-focused coping and symptoms on the PCSS was not. The direct effect of personal control on PCSS scores was not significant. The indirect effect was tested using a bootstrap estimation approach with 5000 samples. The results indicated the indirect coefficient was significant, IE = 2.48, SE = 2.48, 95% CI = .16, 6.35.

Figure 7.

Mediational Analysis of Personal Control, Problem-focused Coping, and PCSS

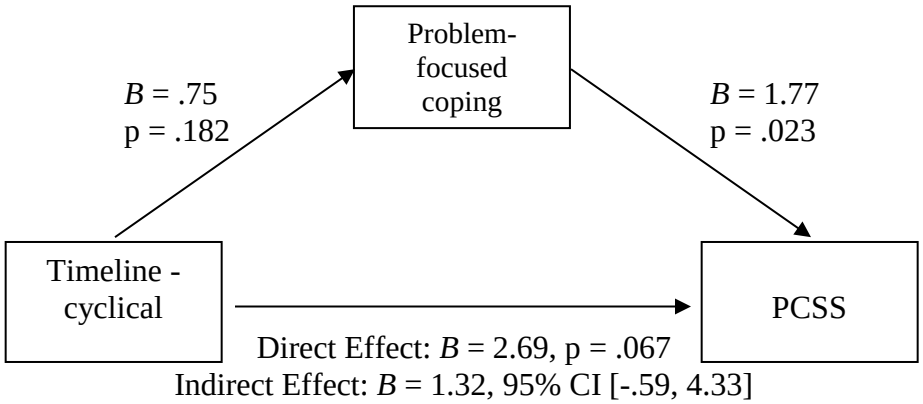


The relationship between timeline-cyclical and symptoms on the PCSS was not mediated by problem-focused coping. As Figure 8 illustrates, the standardized regression coefficient between timeline cyclical and problem-focused coping was not statistically significant, whereas the standardized regression coefficient between problem-focused coping and symptoms on the PCSS was significant. The direct effect of timeline-cyclical beliefs on PCSS scores approached significance (p = .067). The indirect effect was tested using a bootstrap estimation approach with

5000 samples. The results indicated the indirect coefficient was not significant, IE = 1.32, SE = 1.21, 95% CI = -.59, 4.33.

Figure 8.

Mediational Analysis of Timeline-cyclical, Problem-focused Coping, and PCSS



Overall, the hypothesis that coping strategies would partially mediate the relationship between illness representations and poor outcome was partially supported. As expected, approach coping strategies were found to partially mediate the relationships between some aspects of illness representations (personal control beliefs) and poor outcome; however, this relationship was only found for the outcome variable of PCSS symptoms, not anxiety symptoms. Also consistent with predictions, a number of correlations were identified between aspects of illness representations, coping strategies, and outcome variables. More specifically, correlations were identified between cyclical timeline beliefs and both PCSS and anxiety symptoms, as well as between personal control beliefs and PCSS symptoms. With respect to coping strategies, only problem-focused coping strategies were correlated with outcome, and only with PCSS symptoms.

CHAPTER 5

DISCUSSION

The goal of the current study was to add to the body of literature examining outcome following mild TBI. The purpose of this study was two-fold. The first aim of the study was to further the understanding of the increased vulnerability to acquired anxiety disorders seen following mild TBI. The second purpose of this study was to explore possible mediational relationships between illness representations, coping styles, and outcome in an acutely concussed athlete group.

Based on analyses from a subset of concussed athletes, there was some indication of poor affective outcome in this group following concussion. As expected, concussed athletes' scores on a measure of post-concussion symptoms increased from pre- to post-injury, with a trend towards higher levels of stress and anxiety within this small group. There were no differences in pre- and post-injury levels of depressive symptoms in this sample of concussed athletes. A study conducted by Mainwaring and colleagues (2004) revealed that levels of depression were elevated following sports-concussion at 4 days post-injury but had resolved by 1 week post-injury. Given that the concussed athletes in the current study were seen between 3 and 52 days post-injury, acutely elevated levels of depression may have been missed. These findings suggest that post-concussion anxiety and stress are important issues for continued research. The implications of the various physiological and psychological variables on poor outcome examined in the current study are discussed below.

Classical Conditioning/Associative Learning

Acquisition and Extinction

One of the aims of the present study was to extend classical conditioning findings in brain-injured rodents to a human population with mild TBI by examining affective associative learning (both aversive and pleasant) in concussed individuals and healthy controls. As predicted, there were no differences between concussed athletes and healthy controls in either the pleasant or aversive conditioning tasks during the pre-acquisition phase with regards to expectancy ratings, heart rate response, skin conductance response, or reaction time to the conditioned stimulus.

Based on rodent models showing greater aversive conditioning following mild TBI, it was predicted that concussed athletes would demonstrate greater associative learning during the acquisition (learning) phase than healthy controls; however, this was largely unsupported in the present study. Contrary to predictions, there were no differences in number of trials to reach 100% expectancy, average expectancy ratings, or autonomic response to the conditioned stimulus. However, concussed athletes had faster reaction times to the conditioned stimulus than healthy controls during the acquisition phase of the aversive conditioning task. During the pleasant conditioning task, there were no differences between the two groups on any of these measures. Similarly, the hypothesis that expectancy ratings of the conditioned stimulus and number of trials to reach extinction (-100%) would differ between the two groups during the extinction phase was not supported. Whereas some studies of aversive conditioning in anxiety disorders have demonstrated greater resistance to extinction in this population (e.g., Orr et al. 2000), at least one study has found greater fear conditioning without associated differences in extinction (Glenn et al., 2017). Interestingly, in the current study, concussed athletes

demonstrated higher average expectancy ratings to the conditioned stimulus than healthy controls during the generalization phase in both the aversive and pleasant conditioning tasks.

The combination of faster reaction time during the acquisition phase and the higher expectancy ratings during the generalization phase to the conditioned stimulus in the aversive task, and the higher expectancy ratings to the conditioned stimulus during the generalization phase in the pleasant task, suggest that associative learning may differ between concussed athletes and healthy controls in some way. It is unclear why differences in reaction time and expectancy ratings were not evident during the same phase of the aversive task, but it may be reflective of the level of awareness, wherein reaction times reflect associative strength below a person's level of awareness and expectancy ratings reflect a more conscious level of associative learning. Some authors have examined reaction time as a measure of associative strength, and suggested that it reflects a different learning process than conscious expectancy (Craddock et al., 2012). The time course of these two learning processes may differ, and it may not be surprising that a learning process characterized by reaction time, in which individuals may not explicitly be aware of an association, would precede conscious expectancy, in which individuals are aware that one stimulus predicts another. This could explain why the differences in reaction time were seen prior to differences in expectancy ratings in the current study. However, it is unclear why this pattern was evident in the aversive, but not pleasant task. While the same pattern of faster reaction times by the athletes to the conditioned stimulus was seen in the acquisition phase of the pleasant task in the concussed athletes, this was not significant. One possible explanation for the difference in the two tasks is that it reflects differences in underlying neural circuitry for aversive versus pleasant conditioning tasks; given the amygdala's known function in fear processing and learning, it may be preferentially recruited for aversive conditioning tasks. This would be

consistent with other research demonstrating consistent activation of the amygdala to fearful stimuli and inconsistent activation to happy or pleasant stimuli (e.g., Canli, Sivers, Whitfield, Gotlib, & Gabrieli, 2002). In addition, the well-established role of the amygdala in the unconscious processing of emotional information (e.g., Diano, Celeghin, Bagnis, & Tamietto, 2016) is consistent with the hypothesis that faster reaction times represent a more unconscious type of learning. Future research could test this hypothesis by collecting functional imaging data during these tasks.

The presence of group differences in expectancy ratings in the generalization phases, but not acquisition phases, is somewhat puzzling. One possible explanation involves the difficulty of the task; given that there were only two stimuli in the acquisition phase, this phase of the task was very easy. It is possible that the simplicity of the task created a ceiling effect wherein differences between the concussed athletes and healthy controls could not be detected. The generalization phase, which was a more difficult phase of the task (i.e., 6 different stimuli to differentiate), appears to have been better at differentiating performance between the two groups. Alternatively, it is possible that higher expectancy ratings during the generalization phase reflect increased persistence of the classical conditioning effects learned during the acquisition phase. Consistent with this hypothesis, athletes demonstrated higher expectancy ratings to the first presentation of the conditioned stimulus during both the generalization and extinction phases, although the difference in the extinction phase of the aversive task was not significant. This suggests that concussed athletes demonstrated greater persistence of classical conditioning effects in the context of comparable overall learning and extinction. Of note, all participants completed evaluative ratings of the stimuli between the acquisition and generalization phases, and again between the generalization and extinction phases. It is possible that being asked to

evaluate the stimuli, despite the lack of differences in ratings, acted as a priming event for the concussed athletes but not the controls. To test the hypothesis that the first trials in the generalization and extinction phases acted as a measure of the persistence of classical conditioning effects formed during the acquisition phase, future research may benefit from the inclusion of distractor tasks and examination of expectancy ratings for the conditioned stimulus at immediate and also delayed time points.

It is also important to note that the majority of differences found between the athletes and controls, with the exception of reaction time, were found in both an aversive and pleasant conditioning task. This suggests that abnormal classical conditioning may be evident not only in fear conditioning, but in affective associative learning more generally. To date, the literature examining individuals with anxiety disorders, as well as anxiety in healthy individuals, has focused on aversive conditioning specifically rather than affective classical conditioning more generally (e.g., Buchel, Morris, Dolan, & Friston, 1998; Lissek et al., 2005). Future research in individuals with anxiety disorders to examine possible differences in both aversive and pleasant tasks may further our understanding of the role of classical conditioning more generally.

The lack of findings in heart rate response and skin conductance responses may be explained in a few ways. One possible explanation relates to the qualitative aspects of the unconditioned stimulus. It may not have been sufficiently aversive to result in autonomic system responses; this notion is supported by the fact that none of the mean heart rate responses differed from 0. However, the initial study by Neumann and Waters (2006) suggests that equivalent or superior conditioning effects were seen in skin conductance and heart rate responses when using this stimulus in comparison to both an electric shock and a 100 dB tone. Alternatively, this finding may be explained by potential differences between athletes and non-athletes in

autonomic reactivity. Previous research has suggested that athletes demonstrate lower autonomic responses, at least in heart rate variability, than non-athletes in response to experimental stressors (Rimmele et al, 2007; Rimmele et al., 2009). It is therefore possible that athletes also demonstrate lower heart rate and skin conductance in response to aversive stimuli. This difference would then be masked in a study where concussed athletes are not compared to other, healthy athletes, but rather to a non-athlete group. The autonomic responses in this sample of athletes may actually represent an increase from their baseline responses prior to having sustained a head injury. In addition to differences in autonomic reactivity, the lack of findings may be explained by baseline differences between the groups on psychological variables; while there were no differences between the two groups on measures of anxiety, depressive, or post-concussion scores at baseline, there were differences in their levels of stress, with non-athletes having higher levels at baseline. It is possible then that their autonomic stress response in heart rate and skin conductance was also higher at baseline. Further research may help examine this hypothesis by comparing athlete and non-athlete groups pre- and post-concussion.

A review of 20 studies that demonstrated faster fear learning and more resistance to extinction in anxious versus non-anxious individuals suggested that these effects tend to be modest (Lissek et al, 2005). Therefore, it may not be surprising that only minor differences in classical conditioning were demonstrated in the current study. The presence of even these small differences in a study where concussed athletes and healthy controls had similar levels of anxious symptomatology suggests that future research examining classical conditioning in concussed individuals may be warranted. It is also possible that the small sample size and low power was unable to detect additional differences in some of the measures.

Generalization

Another aspect of classical conditioning is the concept of generalization, in which conditioned responses are observed to novel stimuli that resemble the conditioned stimulus. Rodent models of concussion have demonstrated increased generalization of fear response (e.g. Reger et al., 2012; Almeida-Suhett et al., 2014), and studies examining humans with PTSD have also found greater generalization (Orr et al., 2000). Contrary to predictions, there were no differences between concussed athletes and healthy controls on any of the measures of generalization, including expectancy ratings, autonomic response, and reaction time. The one exception was reaction time to the generalization stimuli in the pleasant task, with concussed athletes demonstrating faster reaction times. The same pattern of faster responding was seen in the aversive task, but the difference was not significant. This may be reflective of poor power in this study due to a small sample size. It is possible that this trend towards faster reaction times to the generalization stimuli by concussed athletes is reflective of an unconscious learning effect taking place prior to more conscious learning processes such as expectancy ratings, similar to that seen in the acquisition phase. It is unclear why an unconscious learning process would not be reflected in autonomic responses, but this may again be due to stimuli that are not sufficiently aversive, or due to differences in autonomic responses between athletes and non-athletes in general.

Cortisol-Related Stress Response

The present study examined differences between concussed athletes and healthy non-athlete controls in baseline cortisol levels, as well as in cortisol-related stress response to an experimental stressor. The results are consistent with previous research generally showing no differences between athletes and healthy controls in baseline cortisol levels (e.g., Cevada,

Vasques, Moraes, & Deslander, 2014; Rimmele et al., 2007; Rimmele et al., 2009; Verner et al., 2010), as well as studies showing no difference between concussed athletes and matched controls at various recovery time points (Hutchison et al., 2017). The results of the present study are also consistent with previous research in finding a significant effect of time (Verner et al., 2010), with cortisol levels decreasing significantly between time 1 and 2, before and after an experimental stressor, in both athlete and non-athlete groups.

The results of the present study, however, are inconsistent with previous research suggesting that athletes demonstrate a less pronounced cortisol-related stress response. Rimmele and colleagues (2007) compared a group of 22 trained "sportsmen" (athletes) with 22 healthy untrained men in their salivary cortisol levels, heart rate, and psychological responses (mood, calmness, anxiety) both before and after a psychosocial laboratory stressor (Tier Social Stress Test). There were no baseline differences in cortisol or heart rate between the groups, but trained men exhibited significantly lower cortisol and heart rate responses to the stressor compared with untrained men. With regards to psychological responses, the trained men also demonstrated significantly higher calmness, better mood, and a trend toward lower state anxiety during the experiment. Rimmele and colleagues (2009) replicated these findings, this time including three groups: elite sportsmen, amateur sportsmen, and untrained men. The same measures were used, and elite sportsmen exhibited significantly lower cortisol, heart rate, and anxiety compared with untrained men. The amateur sportsmen demonstrated significantly reduced heart rate, but no difference in cortisol compared with untrained men. Similarly, Verner and colleagues (2010) found a decreased cortisol response to an experimental stressor in female athletes versus non-athletes. The finding that there were no differences between the two groups in the current study

then, may be reflective of differences between athletes and non-athletes at baseline, rather than a true lack of differences between concussed and non-concussed individuals.

If athletes and non-athletes are indeed different in their cortisol-related stress responses at baseline, the absence of differences in the current study may suggest an increased stress response in concussed athletes compared to their own baseline levels or compared to other, non-concussed, athletes. This would suggest that the concussions sustained by the athletes in this study did have an impact on their cortisol-related stress response; however, this is speculative in the absence of baseline data. Longitudinal studies that examine athletes prospectively and measure cortisol stress responses both pre- and post- head injury may be beneficial in testing this hypothesis. In addition, comparing cortisol-related stress responses across concussed and non-concussed athletes, as well as concussed and non-concussed non-athletes may provide more information in this regard.

Common Sense Model

Examination of possible relationships between illness representations, coping, and outcome revealed that beliefs regarding the cyclical timeline of the injury were not correlated with any coping subscales, but were correlated with symptoms of anxiety. This suggests a possible independent effect of these illness representations on anxiety symptoms. This is not a surprising finding given that these representations are characterized by beliefs about the unpredictable and cyclical nature of symptoms, and that anxiety is often characterized by a fear of unpredictability. It cannot be ruled out, however, that the relationship between cyclical timeline beliefs and symptoms of anxiety occurs in the other direction; more specifically, it may be that individuals who have higher baseline levels of anxious symptomatology are more likely to interpret the symptoms of their injury as unpredictable. Either way, this finding suggests that

the CSM may not be applicable to certain outcome variables where the relationship between illness representation and outcome is more direct.

In terms of mediation relationships, correlations were found between aspects of illness representations, specifically feelings of personal control and beliefs regarding the cyclical timeline of the injury, and post-concussion symptoms. Of the three coping subscales, only approach coping was found to correlate with post-concussive symptoms in this group. This is in contrast with other illness groups where avoidance coping was most often found to act as a partial mediator between illness representations and poor outcome. It is, however, in line with other studies examining the effects of coping on outcome in mild TBI groups where approach coping has been demonstrated to have an effect on outcome, with a pattern of a negative effect seen in early stages of recovery and a positive effect seen in more chronic phases (Snell et al., 2011a). In the early recovery stages following a concussion, more passive coping strategies may be the most appropriate as rest is generally recommended. As recovery progresses and an individual returns to cognitive and physical activities, however, more active coping strategies may become more helpful. This could suggest that the relationship between illness beliefs and poor outcome is mediated by the use of coping strategies that are maladaptive for the recovery of that particular illness or injury, or are maladaptive for the level of recovery within the same illness or injury.

Problem-focused/approach coping was not found to mediate the relationship between cyclical timeline beliefs and outcome, suggesting independent effects of these illness representations on post-concussion symptoms. However, the relationship between personal control beliefs and post-concussion symptoms was partially mediated by problem-focused/approach coping strategies. Although personal control beliefs are generally thought to

have a positive connotation in that they lead to problem-focused or approach type strategies wherein an individual exerts some control over their stressor, they may lead to poor outcomes in an illness group where recovery is more passive in nature, at least in the early stages. The findings of the present study are consistent with Hagger and Orbell's (2003) meta-analysis that found that individuals with greater endorsement of control over the illness were more likely to use adaptive coping strategies such as problem-focused coping, cognitive reappraisal, and seeking social support. These findings are also consistent with the studies of Woodrome et al. (2011), Covassin et al. (2013), and Snell et al. (2011a), who found that approach coping strategies were associated with poor outcomes early after injury when passive recovery is thought to be appropriate. In these studies, avoidance coping strategies were associated with poor outcome when the injury became chronic and more active coping may have beeen necessary; unfortunately, the recruitment of athletes in the chronic stage of recovery was not successful in the present study and thus mediational relationships among these factors could not be examined across the timeline of recovery.

Future research should aim to follow concussed athletes over time to monitor changes in coping strategies and outcome after their injury. This would also allow for the identification of athletes who have prolonged recovery and those who recover quickly, as these are different groups of individuals and may show different patterns of illness representations and coping strategies. Alternatively, cross-sectional studies examining athletes at varying stages of recovery would likely provide some insight in this regard. Overall, the findings of the current study suggest that there may be some utility in applying the Common Sense Model to a mild TBI group. It also suggests that some illness representations may have a more direct relationship with post-concussion symptoms. This may be the case for illness representations that do not lend

themselves as easily to specific coping strategies; whereas beliefs about personal control may easily lend themselves to a coping style characterized by personally approaching and exerting control over the problem, beliefs about other aspects, such as an unpredictable timeline, may not lend themselves as easily to the implementation of a specific coping strategy. Overall, these results underscore the importance of psychoeducation to influence both maladaptive and/or incorrect illness beliefs as well as appropriate coping styles. Previous research has suggested that illness beliefs are most malleable and amenable to change early after an injury, but may become fixed and less malleable with time (Petrie, Cameron, Ellis, Buick, & Weinman, 2002; Snell et al., 2013), indicating the need to identify and educate these individuals early on in an effort to reduce poor outcomes.

Integrating Psychological and Physiological Factors in Understanding Outcome

Understanding recovery after mild TBI, including the resolution of cognitive, somatic, and affective symptoms, remains an important field of inquiry. Silverberg and Iverson's 2011 review of the research within this area suggested that both neurobiological and psychological factors play an important role in the development and maintenance of post-concussion symptoms. Despite this, research on these factors is too often undertaken independently, and not frequently integrated. The present study attempted to address this limitation of previous research by including both physiological and psychological mechanisms of risk for anxiety following concussion specifically. It provides partial support for changes in associative conditioning following concussion, as well as the importance of psychological factors related to illness representations and coping behaviours. It is possible that these represent various pathways to the acquisition of anxiety, or that psychological illness representations and behavioural responses of coping compound a neurobiological risk manifested in structural and functional changes

resulting in dysfunctional associative learning. Future research should continue to consider both physiological and psychological factors and to examine the complex interplay between them.

Study Limitations

The present study had a number of limitations. One of the major limitations was small sample size, and thus limited power. Despite numerous attempts to increase recruitment in this study through increasing reimbursement and using more direct contact methods (e.g., phone calls, text messaging), recruitment remained low. Future research conducted over a longer period of time with higher recruitment rates may be better able to reveal these small effects.

A second limitation in this study was the lack of a physician diagnosis of concussion for all athletes, and variability in time from the concussive injury. While all athletes had an impact with associated cognitive and physical symptoms and were referred by athletic trainers, the lack of physician diagnosis makes these injuries suspected concussions. Many of the concussed athletes were not seen within the 10-day acute stage. Although some differences were found between these concussed athletes and healthy controls, the effect sizes would likely be larger if the concussed athletes were recruited in the acute phase of concussion. Research employing non-human animal models of mild TBI suggests that within 10 days of injury, neurochemical and metabolic levels return to normal (Hovda et al., 1991; Yoshino et al., 1991), and studies examining neuropsychological functioning in humans demonstrate a 10-day recovery curve (Belanger & Vanderploeg, 2005). Thus, including athletes who were more than 10 days post-injury in this study may have influenced the results through the inclusion of concussed athletes who were no longer symptomatic and had likely already recovered. It should be noted, however, that despite this variability, the athlete group did have significantly higher post-concussion symptoms than the control group, suggesting that the athlete group was symptomatic overall. In

addition, correlational analyses failed to reveal a relationship between days since injury and the variables of interest in this study, although lack of power likely played a role. Future research, however, should only include athletes who are acutely concussed, or separate concussed individuals into acute and chronic groups.

An additional limitation in this study is that concussed athletes were compared to healthy non-athletes rather than healthy athletes. Given baseline differences between athletes and the general population, it would be prudent to control for these differences by comparing athletes with and without concussion, as well as non-athletes with and without concussion. Alternatively, while the current study was limited by small sample size and technical difficulties, baseline differences could be controlled for statistically.

Lastly, future research in this area should design classical conditioning tasks that are more difficult than the tasks in the present study to reduce the risk of ceiling effects in learning, and possibly demonstrate small effects. In addition, the stimuli in this study may not have been sufficiently aversive to demonstrate small differences in associative learning between athletes and controls. Interestingly, qualitative observations by some research assistants suggested that at least some of the participants found the sound of a baby laughing in the pleasant task to be equally aversive to the sound used in the aversive task. The inclusion of a subjective rating scale of the two sounds would have been helpful in this regard. Future research using both pleasant and aversive conditioning tasks should employ these types of ratings to ensure the validity of the stimuli used.

Strengths of Study

The present study had a number of strengths. One major strength was that it explored risk of anxiety disorders following concussion using behavioural, psychological, and physiological

methods within the Common Sense Model and classical conditioning paradigms, thereby providing information about various possible avenues through which this risk may manifest. It also used a number of measures to examine associative learning in particular (i.e., objective ratings of expectancy, reaction time, and physiological responses), which allowed for the identification of some changes in learning in the context of comparable performance in other aspects of learning. Aversive conditioning has been shown to be an important process in the development and maintenance of anxiety disorders, and to be reliant on a number of brain structures vulnerable to the effects of concussion. Examining differences in aversive conditioning provides a novel way of understanding the risk for increased anxiety following concussion.

While the majority of studies that examine classical conditioning within the context of anxiety disorders have used only an aversive stimulus, this study used both an aversive learning task as well as a task that combined a neutral stimulus with a pleasant stimulus. Research employing a classical conditioning paradigm in the study of anxiety disorders in human populations and fear behaviours in brain-injured rats has focused exclusively on the associative learning between a neutral and fear-inducing or aversive stimulus, while largely ignoring possible pleasant or appetitive conditioning. Similarly, research on classical conditioning in anxiety disorders in humans has been extensive for fear conditioning but not appetitive conditioning, where the research has been largely restricted to its implications on addiction and obesity. By including both types of affective conditioning in the present study, it was possible to examine whether concussed athletes demonstrated overall differences in affective classical conditioning, or demonstrated differences only when the learning involved an aversive stimulus.

The fact that these two types of conditioning were so similar in the present study is an interesting finding and reveals new avenues for research in this area.

Conclusions

The goal of the current study was to add to the understanding of poor outcome following mild TBI, particularly with respect to the increased risk for anxiety disorders. This study took an important first step in extending research on aversive conditioning in brain-injured rats to a human population. Differences in aversive conditioning were proposed as a possible mechanism through which concussed individuals may be at risk for anxiety disorders. The results of the present study partially supported this hypothesis, thereby providing important insights into the possible etiology of these disorders following concussion. These findings provide new and exciting directions for future research, particularly if functional imaging techniques can be used to correlate potential differences in aspects of classical conditioning with underlying brain structures and function. By increasing our understanding of the etiology of acquired anxiety disorders in concussed populations we can improve our strategies for preventing these disorders and for providing appropriate interventions.

The current study also examined illness representations, coping strategies, and outcome, and provided some support for employing the Common Sense Model within a population of concussed individuals. Understanding these relationships can help guide intervention strategies for individuals following a concussion to improve outcomes. The finding that active coping strategies may actually be associated with poor outcome in acutely concussed or recently concussed individuals is an important one, as it goes against the majority of research with healthy individuals or other injured or ill populations where active coping strategies are generally associated with better outcome. This highlights the unique nature of the recovery process in

concussion, where passive strategies may be more appropriate, at least in the early phases. Psychoeducation regarding the best type of coping strategies to use following a concussion may be beneficial. The finding of direct effects of certain illness representations, particularly cyclical timeline beliefs, on poor outcome also suggests that this population may benefit from psychoeducation that emphasizes the generally short and positive recovery time period for these individuals. As suggested by previous research, this type of psychoeducation would be best employed as soon as possible after an individual sustains a concussion, when illness beliefs tend to be most easily modified (Petrie et al., 2002).

Overall, the current study found some evidence to support differences between concussed athletes and control participants in some aspects of classical conditioning, as well as evidence to support the use of the Common Sense Model in mild TBI populations. Future research to replicate and build on these findings, in order to increase our understanding of the etiology, maintenance, and treatment of poor outcome following concussion may be beneficial.

REFERENCES

Alexander, A.L., Lee, J. E., Lazar, M, & Field, A.S. (2007). Diffusion tensor imaging of the brain. *Neurotherapeutics, 4*(3), 316-329.

Almeida-Suhett, C.P., Prager, E.M., Pidoplichko, V., Figueiredo, T.H., Marini, A.M., Li, Z., … Braga, M.F.M. (2014). Reduced GABAergic inhibition in the basolateral amygdala and the development of anxiety-like behaviors after mild traumatic brain injury. *Public Library of Science, 9*(7), 1-13.

American Psychiatric Association. (2000). Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.). Washington, DC: Author.

Andreatta, M., & Pauli, P. (2015). Appetitive vs. aversive conditioning in humans. *Frontiers in behavioral neuroscience, 9.* Anson, K. & Ponsford, J. (2006). Coping and emotional adjustment following traumatic brain injury. *Journal of Head Trauma Rehabilitation, 21*(3), 248-259.

Antony, M. M., Bieling, P. J., Cox, B. J., Enns, M. W., & Swinson, R. P. (1998). Psychometric properties of the 42-item and 21-item versions of the Depression Anxiety Stress Scales in clinical groups and a community sample.Psychological Assessment, 10(2), 176.

Bazarian, J. J., Blyth, B., Mookerjee, S., He, H., & McDermott, M. P. (2010). Sex differences in outcome after mild traumatic brain injury. *Journal of Neurotrauma, 27*(3), 527-539.

Bazarian, J.J., Donnelly, K., Peterson, D.R., Warner, G.C., Zhu, T., & Zhong, J. (2013). The relation between posttraumatic stress disorder and mild traumatic brain injury acquired during operations enduring freedom and Iraqi freedom. *Journal of Head Trauma Rehabilitation, 28,* 1-12.

Bazarian, J. J., Zhong, J., Blyth, B., Zhu, T., Kavcic, V., & Peterson, D. (2007). Diffusion tensor imaging detects clinically important axonal damage after mild traumatic brain injury: a pilot study. *Journal of Neurotrauma, 24*(9), 1447-1459.

Belanger, H.G., Curtiss, G., Demery, J.A., Lebowitz, B.K., & Vanderploeg, R.D. (2005). Factors moderating neuropsychological outcomes following mild traumatic brain injury: A meta-analysis. *Journal of the International Neuropsychological Society, 11*(3), 215-227.

Belanger, H.G. & Vanderploeg, R.D. (2005). The neuropsychological impact of sports-related concussion: A meta-analysis. *Journal of the International Neuropsychological Society, 11*(4), 345-357.

Belanger, H.G., Vanderploeg, R.D., Curtiss, G., & Warden, D.L. (2007). Recent neuroimaging techniques in mild traumatic brain injury. *Journal of Neuropsychiatry and Clinical Neuroscience, 19*(1), 5-20.

Bergsneider, M., Hovda, D.A., McArthur, D.L., Etchepare, M., Huang, S.C., Sehati, N., …, Becker, D.P. (2001). Metabolic recovery following human traumatic brain injury based on FDG-PET: Time course and relationship to neurological disability. *Journal of Head Trauma Rehabilitation, 16*, 135-148.

Bigler, E.D. (2008). Neuropsychology and clinical neuroscience of persistent post-concussive syndrome. *Journal of the International Neuropscyhological Society, 14*, 1-22.

Bigler, E.D. & Maxwell, W.L. (2012). Neuropathology of mild traumatic brain injury: Relationship to neuroimaging findings. *Brain Imaging Behavior, 6*, 108-136.

Bigler, E.D., Farrer, T.J., Pertab, J.L., James, K., Petrie, J.A., & Hedges, D.W. (2013). Reaffirmed limitations of meta-analytic methods in the study of mild traumatic brain injury: A response to Rohling et al. *Clinical Neuropsychology, 27*(2), 176-214.

Binder, L.M. (1986). Persisting symptoms after mild head injury: A review of the postconcussive syndrome. *Journal of Clinical and Experimental Neuropsychology, 8,* 323-346.

Binder, L.M., Rohling, M.L., & Larrabee, G.J. (1997). A review of mild head trauma. Part I: Meta-analytic review of neuropsychological studies. *Journal of Clinical and Experimental Neuropsychology, 19,* 421-431.

Boake, C., McCauley, S.R., Levin, H.S., Pedroza, C., Contant, C.F., Song, J.X., …, Diaz-Marchan, P.J. (2005). Diagnostic criteria for postconcussional syndrome after mild to moderate traumatic brain injury. *Journal of Neuropsychiatry and Clinical Neuroscience, 17*(3), 350-356.

Bradley, M.,M. & Lang, P.J. (2007). The International Affective Digitized Sounds 2nd Edition (IADS-2). National Center for the Study of Emotion and Attention.

Bremner, J.D., Staib, L.H., Kaloupek, D., Southwick, S.M., Soufer, R., & Charney, D.S. (1999). Neural correlates of exposure to traumatic pictures and sound in Vietnam combat veterans with and without posttraumatic stress disorder: A positon emission tomography study. *Biological Psychiatry, 45,* 806-816.

Broglio, S.P., Eckner, J.T., Surma, T., & Kutcher, J.S. (2011). Post-concussion cognitive declines and symptomatology are not related to concussion biomechanics in high school football players. *Journal of Neurotrauma, 28,* 2061-2068.

Broglio, S.P., Schnebel, B., Sosnoff, J.J., Shin, S., Feng, X., He, X., & Zimmerman, J. (2010). The biomechanical properties of concussions in high school football. *Medical Science of Sports Exercise, 42,* 2064-2071.

Browne, K.D., Chen, X., Meaney, D.F., & Smith, D.H. (2011). Mild traumatic brain injury and diffuse axonal injury in swine. *Journal of Neurotrauma, 28*(9), 1747-1755.

Bryant, R.A. (2001). Posttraumatic stress disorder and mild brain injury: controversies, causes, and consequences. *Journal of Clinical and Experimental Neuropsychology, 23,* 718-728.

Bryant, R.A. (2008). Disentangling mild traumatic brain injury and stress reactions. *New England Journal of Medicine, 358,* 525-527.

Buchel, C., Morris, J., Dolan, R.J., & Friston, K.J. (1998). Brain systems mediating aversive conditioning: An event-related fMRI study. *Neuron, 20*(5), 947-957.

Canli, T., Sivers, H., Whitfield, S. L., Gotlib, I. H., & Gabrieli, J. D. (2002). Amygdala response to happy faces as a function of extraversion. *Science, 296*(5576), 2191-2191.

Carlisle, A., John, A. M., Fife-Schaw, C., & Lloyd, M. (2005). The self-regulatory model in women with rheumatoid arthritis: Relationships between illness representations, coping strategies, and illness outcome. *British Journal of Health Psychology, 10*(4), 571-587.

Carroll, L.J., Cassidy, J.D., Peloso, P.M., Borg, J., von Holst, H., Holm, L., …, Pepin. M. (2004). Prognosis for mild traumatic brain injury: Results of the WHO collaborating centre task force on mild traumatic brain injury. *Journal of Rehabilitation Medicine, 43,* 84-105.

Carver, C.S. (1997). You want to measure coping, but your protocol's too long: Consider the Brief COPE. *International Journal of Behavioral Medicine, 4*(1), 92-100.

Centers for Disease Control and Prevention. (2004). Heads up: Facts for physicians about mild traumatic brain injury (MTBI). Available online at: url: http://www.cdc. gov/Migrated_Content/Brochures_and_Catalogs/tbi_ mtbi_facts_for_physicians.pdf

Centers for Disease Control and Prevention. (2016, February 08). Injury Prevention & Control: Traumatic Brain Injury & Concussion. Retrieved January 06, 2017, from https://www.cdc.gov/traumaticbraininjury/severe.html

Cevada, T., Vasques, P. E., Moraes, H., & Deslandes, A. (2014). Salivary cortisol levels in athletes and nonathletes: a systematic review. *Hormone and Metabolic Research, 46*(13), 905-910.

Chappell, M.H., Ulug, A.M., Zhang, L., Heitger, M.H., Jordan, B.D., Zimmerman, R.D., & Watts, R. (2006). Distribution of microstructural damage in the brains of professional boxers: A diffusion MRI study. *Journal of Magnetic Resonance Imaging, 24,* 537-542.

Cohen, B.A., Inglese, M., Rusinek, H., Babb, J.S., Grossman, R.I., & Gonen, O. (2007). Proton MR spectroscopy and MRI-volumetry in mild traumatic brain injury. *American Journal of Neuroradiology, 28,* 907-913.

Covassin, T., Elbin, R.J., Crutcher, B., Burkhart, S., & Kontos, A. (2013). The relationship between coping, neurocognitive performance, and concussion symptoms in high school and collegiate athletes. *The Sport Psychologist, 27,* 372-379.

Craddock, P., Molet, M., & Miller, R. R. (2012). Reaction time as a measure of human associative learning. *Behavioural processes, 90*(2), 189-197.

Curran, C.A., Ponsford, J.L. & Crowe, S. (2000). Coping strategies and emotional outcome following traumatic brain injury: A comparison with orthopedic patients. *Journal of Head Trauma Rehabilitation, 15*(6), 1256-1274.

Davey, G.C. (1992). Classical conditioning and the acquisition of human fears and phobias: A review and synthesis of the literature. *Advances in Behaviour Research and Therapy, 14,* 29-66.

De Beaumont, L., Theoret, H., Mongeon, D., Messier, J., Leclerc, S., Tremblay, S., …, Lassonde, M. (2009). Brain function decline in healthy retired athletes who sustained their last sports concussion in early adulthood. *Brain, 132,* 695-708.

Deckersbach, T., Dougherty, D.D., & Rauch, S.L. (2006). Functional imaging of mood and anxiety disorders. *Journal of Neuroimaging, 16,* 1-10.

DeFord, S. M., Wilson, M. S., Rice, A. C., Clausen, T., Rice, L. K., Barabnova, A., ... & Hamm, R. J. (2002). Repeated mild brain injuries result in cognitive impairment in B6C3F1 mice. *Journal of Neurotrauma*, *19*(4), 427-438.

de Sousa, A., McDonald, S., & Rushby, J. (2012). Changes in emotional empathy, affective responsivity, and behavior following severe traumatic brain injury. Journal of clinical and experimental neuropsychology, 34(6), 606-623.

Diano, M., Celeghin, A., Bagnis, A., & Tamietto, M. (2016). Amygdala response to emotional stimuli without awareness: facts and interpretations. *Frontiers in psychology*, *7*.

Diefenbach, M. A., & Leventhal, H. (1996). The common-sense model of illness representation: Theoretical and practical considerations. *Journal of Social Distress and the Homeless*, *5*(1), 11-38.

Edgar, K. A., & Skinner, T. C. (2003). Illness representations and coping as predictors of emotional well-being in adolescents with type 1 diabetes. *Journal of Pediatric Psychology*, *28*(7), 485-493.

Edna, T.H. & Cappelen, J. (1987). Late postconcussional symptoms in traumatic brain injury: An analysis of frequency of risk factors. *Acta Neurochirurgica, 86,* 1-12.

Ehmed, S.L. & Sullivan, K.A. (2015). Diagnostic terminology is not associated with contact-sport players' expectations of outcome from mild traumatic brain injury. *Brain Injury*. Advance online publication. doi: 10.3109/02699052.2014.998709

Eierud, C., Craddock, R.C., Fletcher, S., Aulakh, M., King-Casas, B., Kuehl, D., & LaConte, S.M. (2014). Neuroimaging after mild traumatic brain injury: Review and meta-analysis. *Neuroimage: Clinical, 4,* 283-294.

Epsein, R.S., & Ursano, R.J. (1994). Anxiety Disorders. In: Silver, J.M., Yudofsky, S.C., & Hales, R.E. (Eds.), *Neuropsychiatry of Traumatic Brain Injury* (3-41). Washington, DC: American Psychiatric Press, Inc.

Erlanger, D., Kaushik, T., Cantu, R., Barth, J. T., Broshek, D. K., Freeman, J. R., & Webbe, F. M. (2003). Symptom-based assessment of the severity of a concussion. *Journal of neurosurgery*, *98*(3), 477-484.

Etkin, A. & Wager, T.D. (2007). Functional neuroimaging of anxiety: A meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. *American Journal of Psychiatry, 164,* 1476-1488.

Evans, D., & Norman, P. (2009). Illness representations, coping and psychological adjustment to Parkinson's disease. *Psychology and Health*, *24*(10), 1181-1196.

Faul, M., Xu, L., Wald, M., & Coronado, V. (2010). *Traumatic brain injury in the United States: Emergency department visits, hospitalizations, and deaths 2002-2006.* Atlanta, GA: Centers for Disease Control and Prevention.

Fendt, M. & Fanselow, M.S. (1999). The neuroanatomical and neurochemical basis of conditioned fear. *Neuroscience and Biobehavioral Reviews, 23,* 743-760.

Finset, A. & Andersson, S. (2000). Coping strategies in patients with acquired brain injury: Relationships between coping, apathy, depression and lesion location. *Brain Injury, 14*(10), 887-905.

Frencham, K.A.R., Fox, A.M., & Maybery, M.T. (2005). Neuropsychological studies of mild traumatic brain injury: A meta-analytic review of research since 1995. *Journal of Clinical and Experimental Neuropsychology, 27,* 334-351.

Genovese, R.F., Simmons, L.P., Ahlers, S.T., Maudlin-Jeronimo, E., Dave, J.R., & Boutte, A.M. (2013). Effects of mild TBI from repeated blast overpressure on the expression and extinction of conditioned fear in rats. *Neuroscience, 254,* 120-129.

Gerberding, J.L. & Binder, S. (2003). *Report to Congress on mild traumatic brain injury in the United States: Steps to prevent a serious public health control.* Atlanta, GA: Centers for Disease Control and Prevention.

Giza, C.C. & Hovda, D.A. (2014). The new neurometabolic cascade of concussion. *Neurosurgery, 75,* S24-S33.

Glenn, D. E., Acheson, D. T., Geyer, M. A., Nievergelt, C. M., Baker, D. G., & Risbrough, V. B. (2017). Fear learning alterations after traumatic brain injury and their role in development of posttraumatic stress symptoms. *Depression and anxiety*.

Gordon, W. A., Haddad, L., Brown, M., Hibbard, M. R., & Sliwinski, M. (2000). The sensitivity and specificity of self-reported symptoms in individuals with traumatic brain injury. Brain Injury, 14(1), 21-33.

Gould, R. V., Brown, S. L., & Bramwell, R. (2010). Psychological adjustment to gynaecological cancer: Patients' illness representations, coping strategies and mood disturbance. *Psychology and Health*, *25*(5), 633-646.

Greenwald, RM., Gwin, J.T., Chu, J.J., & Crisco, J.J. (2008). Head impact severity measures for evaluating mild traumatic brain injury risk exposure. *Neurosurgery, 62*(4), 789-798.

Grupe, D.W. & Nitschke, J.B. (2013). Uncertainty and anticipation in anxiety: An integrated neurobiological and psychological perspective. *Nature Reviews Neuroscience, 14,* 488-501.

Gunnar, M. R. (2001). The role of glucocorticoids in anxiety disorders: A critical analysis. *The developmental psychopathology of anxiety*, 143-159.

Guskiewicz, K.M., Marshall, S.W., Bailes, J., McCrea, M., Cantu, R.C., Randolph, C., & Jordan, B.D. (2005). Association between recurrent concussion and late-life cognitive impairment in retired professional football players. *Neurosurgery, 57*, 719-726.

Guskiewicz, K.M., Marshall, S.W., Bailes, J., McCrea, M., Harding, H.P., Matthews, A., …, Cantu, B.C. (2007a). Recurrent concussion and risk of depression in retired professional fooball players. *Medical Science of Sports Exercise, 39*, 903-909.

Guskewiecz, K.M., McCrea, M., Marshall, S.W., Cantu, R.C., Randolph, C., Barr, W., …, Kelly, J.P. (2003). Cumulative effects associated with recurrent concussion in collegiate football players: the NCAA concussion study. *JAMA, 290*(19), 2549-2555.

Guskiewicz, K.M., Mihalik, J.P., Shankar, V., Marshall, S.W., Crowell, D.H., Oliaro, S.M., …, Hooker, D.N. (2007b). Measurement of head impacts in collegiate football players: Relationship between head impact biomechanics and acute clinical outcome after concussion. *Neurosurgery, 61,* 1244-1253.

Hagger, M.S., Chatzisrantis, N.L.D., Griffin, M., & Thatcher, J. (2005). Injury representations, coping, emotions, and functional outcomes in athletes with sports-related injuries: A test of self-regulation theory. *Journal of Applied Social Psychology, 35*(11), 2345-2374.

Hagger, M.S. & Orbell, S. (2003). A meta-analytic review of the common-sense mode of illness representations. *Psychology and Health*, *18*(2), 141-184.

Hayes, A.F. (2013). *Introduction to mediation, moderation, and conditional process analysis: A regression-based approach*. New York, NY: The Guilford Press.

Hayes, J.P., LaBar, K.S., McCarthy, G., Selgrade, E., Nasser, J., Dolcos, F., & Morey, R.A. (2011). Reduced hippocampal and amygdala activity predicts memory distortions for trauma reminders in combat-related PTSD. *Journal of Psychiatry Research, 45*(5), 660-669.

Heldt, S.A., Elberger, A.J., Deng, Y., Guley, N.H., Del Mar, N., Rogers, J., …, Reiner, A. (2014). A novel closed-head model of mild traumatic brain injury caused by primary overpressure blast to the cranium produces sustained emotional deficits in mice. *Frontiers in Neurology, 5*(2), 1-14.

Henry, J. D., & Crawford, J. R. (2005). The short-form version of the Depression Anxiety Stress Scales (DASS-21): Construct validity and normative data in a large non-clinical sample. British Journal of Clinical Psychology,44(2), 227-239.

Henry, L.C., Tremblay, S., Boulanger, Y., Ellemberg, D., & Lassonde, M. (2010). Neurometabolic changes in the acute phase after sports concussions correlate with symptom severity. *Journal of Neurotrauma, 27*(1), 65-76.

Hiott, D.W. & Labbate, L. (2002). Anxiety disorders associated with traumatic brain injuries. *NeuroRehabilitation, 17*(4), 345-355.

Hoge, C.W., McGurk, D., Thomas, J.L., Cox, A.L., Engel, C.C., & Castro, C.A. (2008). Mild traumatic brain injury in US soldiers returning from Iraq. *New England Journal of Medicine, 358,* 453-463.

Holzschneider, K. & Mulert, C. (2011). Neuroimaging in anxiety disorders. *Dialogues in Clinical Neuroscience, 13*(4), 453- 461.

Horne, R. & Weinman, J. (2002). Self-regulation and self-management in asthma: Exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. *Psychology and Health, 17,* 17-32.

Hovda, D.A., Yoshino, A., Kawamata, T., Katayama, Y., & Becker, D.P. (1991). Diffuse prolonged depression of cerebral oxidative metabolism following concussive brain injury in the rat: A cytochrome oxidase histochemistry study. *Brain Research, 567,* 1-10.

Hua Li, H., Lee, S. M., Cai, Y., Sutton, R. L., & Hovda, D. A. (2004). Differential gene expression in hippocampus following experimental brain trauma reveals distinct features of moderate and severe injuries. *Journal of Neurotrauma*, *21*(9), 1141-1153.

Hutchison, M. G., Mainwaring, L., Senthinathan, A., Churchill, N., Thomas, S., & Richards, D. (2017). Psychological and physiological markers of stress in concussed athletes across recovery milestones. *The Journal of head trauma rehabilitation*, *32*(3), E38-E48.

Indovina, I., Robbins, T.W., Nunez-Elizalde, A.O., Dunn, B.D., & Bishop, S.J. (2011). Fear conditioning mechanisms associated with trait vulnerability to anxiety in humans. *Neuron, 69*(3), 563-571.

Iverson, G. (2007). Predicting slow recovery from sport-related concussion: The new simple-complex distinction. *Clinical Journal of Sports Medicine, 17*(1), 31-37.

Jasnow, A.M., Ehrlich, D.E., Choi, D.C., Dabrowska, J., Bowers, M.E., McCullough, K.M., … Ressler, K.J. (2013). Thy1-expressing neurons in the basolateral amygdala may mediate fear inhibition. *Journal of Neuroscience, 33*(25), 10396-10404.

Joyce, A.S., LaBella, C.R., Carl, R.L., Lai, J.S., & Zelco, F.A. (2014). The postconcussion symptom scale: Utility of a three-factor structure. *Medical Science Sports Exercise.* Advance online publication doi: 25268538

Kay T, Harrington DE, Adams R, Mild Traumatic Brain Injury Committee, American Congress of Rehabilitation Medicine, Head Injury Interdisciplinary Special Interest Group. Definition of mild traumatic brain injury. Journal of Head Trauma Rehabilitation 1993; 8: 86–87.

Keatley, E., d'Alfonso, A., Abeare, C., Keller, A., & Bertelsen, N.S. (2015). Health outcomes of traumatic brain injury among refugee survivors of torture. *Journal of Head Trauma Rehabilitation.* Advance online publication doi: 25629258/Health-Outcomes-of-Traumatic-Brain-Injury-Among-Refugee-Survivors-of-Torture

Keshavan, M.S., Channabasavanna, S.M., & Reddy, G.N. (1981). Post-traumatic psychiatric disturbances: Patterns and predictors of outcome. *British Journal of Psychiatry, 138,* 157-160.

King, N.S. (1996). Emotional, neuropsychological, and organic factors: Their use in the prediction of persisting postconcussion symptoms after moderate and mild head injuries. *Journal of Neurology, Neurosurgery, and Psychiatry, 61,* 75-81.

King, N.S. (2003). Post-concussion syndrome: Clarity amid the controversy? *British Journal of Psychiatry, 183,* 276-278.

King, N. S., Crawford, S., Wenden, F. J., Moss, N. E. G., & Wade, D. T. (1995). The Rivermead Post Concussion Symptoms Questionnaire: a measure of symptoms commonly experienced after head injury and its reliability. *Journal of neurology, 242*(9), 587-592.King, N.S. & Kirwilliam, S. (2011). Permanent post-concussion symptoms after mild head injury. *Brain Injury, 25*(5), 462-470.

Klucken, T., Kagerer, S., Schweckendiek, J., Tabbert, K, Vaitl, D., & Stark, R. (2009). Neural, eletrodermal, and behavioral response patterns in contingency aware and unaware subjects during a picture-picture conditioning paradigm. *Neuroscience, 158*(2), 721-731.

Kluver, H. & Bucy, P.C. (1939). Preliminary analysis of the temporal lobes in monkeys. *Biological Psychiatry, 42*, 461-471.

Knibb, R. C., & Horton, S. L. (2008). Can illness perceptions and coping predict psychological distress amongst allergy sufferers?. *British Journal of Health Psychology, 13*(1), 103-119.

Kontos, A.P., Elbin, R.J., Appaneal, R.N., Covassin, T., & Collins, M.W. (2013). A comparison of coping responses among high school and college athletes with concussion, orthopedic injuries, and healthy controls. *Research in Sports Medicine, 21*, 367-379.

Kontos, A. P., Elbin, R. J., Schatz, P., Covassin, T., Henry, L., Pardini, J., & Collins, M. W. (2012). A revised factor structure for the post-concussion symptom scale baseline and postconcussion factors. *The American Journal of Sports Medicine*, doi: 0363546512455400.

Koponen, S., Taiminen, T, Portin, R., Himanen, L., Isoniemi, H., Heinonen, …, Tenovuo, O. (2002). Axis I and II psychiatric disorders after traumatic brain injury: A 30-year follow-up study. *American Journal of Psychiatry, 159,* 1315-1321.

Kraus, F. & Chu, L.D. (2005). Epidemiology. In Silver, J.M., McAllister, T.W., & Yudofsky, S.C. (Eds.), *Textbook of Traumatic Brain Injury* (3-26). Washington, DC: American Psychiatric Publishing.

Landre, N., Poppe, C.J., Davis, N., Schmaus, B., & Hobbs, S.E. (2006). Cognitive functioning and postconcussive symptoms in trauma patients with and without mild TBI. *Archives of Clinical Neuropsychology, 21*(4), 255-273.

Lange, R.T., Iverson, G.L., & Rose, A. (2011). Depression strongly influences postconcussion symptom reporting following mild traumatic brain injury. *Journal of Head Trauma Rehabilitation, 26*(2), 127-137.

Langlois, J., Rutland-Brown, W., Wald, M. (2006). The epidemiology and impact of traumatic brain injury: A brief overview. *Journal of Head Trauma Rehabilitation, 21*(5), 375-378.

Larson, E. B., Kondiles, B. R., Starr, C. R., & Zollman, F. S. (2013). Postconcussive complaints, cognition, symptom attribution and effort among veterans. *Journal of the International Neuropsychological Society*, *19*(01), 88-95.

Lau, J.Y., Lissek, S., Nelson, E.E., Lee, Y., Roberson-Nay, R., Poeth, K., …, Pine, D.S. (2008). Fear conditioning in adolescents with anxiety disorders: Results from a novel experimental paradigm. *Journal of the American Academy of Child and Adolescent Psychiatry, 47*(1), 94-102.

Lazarus, R. S. (1993). Coping theory and research: past, present, and future. *Psychosomatic medicine*, *55*(3), 234-247.

Lazarus, R.S. & Folkman, S. (1984). *Stress, appraisal and coping.* New York: Springer.

Leddy, J.J., Kozlowski, K., Donnelly, J.P., Pendergast, D.R., Epstein, L.H., & Willer, B. A preliminary study of subsymptom threshold exercise training for refractory post-concussion syndrome. *Clinical Journal of Sports Medicine, 20*(1), 21-27.

Leventhal, H., Leventhal, E., & Contrada, R. (1998). Self-regulation, health, and behaviour: a perceptual-cognitive approach. *Psychology and Health, 13,* 717-733.

Liberzon, I. & Sripada, C.S. (2008). The functional neuroanatomy of PTSD: A critical review. *Progressive Brain Research, 167,* 151-169.

Lidvall, H.F., Linderoth, B., & Norlin, B. (1974). Causes of the post-concussional syndrome. *Acta Neurologica Scandinavica, 56,* 1-144.

Lifshitz, J., Witgen, B.M., & Grady, M.S. (2007). Acute cognitive impairment after lateral fluid percussion brain injury recovers by one month: Evaluation by conditioned fear response. *Behavior and Brain Research, 177*(2), 347-357.

Linz, D., Penrod, S., & Leventhal, H. (1982). Cognitive organisation of disease among laypersons. Paper presented at the 20th International Congress of Applied Psychology, Edinburgh, Scotland.

Lishman, W. (1988). Physiogenesis and psychogenesis in the 'post-concussional syndrome.' *British Journal of Psychiatry, 153*(4), 460-469.

Lissek, S., Rabin, S., Heller, R.E., Lukenbaugh, D., Geraci, M., Pine, D.S., & Grillon, C. (2010). Overgeneralization of conditioned fear as a pathogenic marker of panic disorder. *American Journal of Psychiatry, 167*(1), 47-55.

Lissek, S., Powers, A.S., McClure, E.B., Phelps, E.A., Woldehawariat, G., Grillon, C., & Pine, D.S. (2005). Classical fear conditioning in the anxiety disorders: A meta-analysis. *Behavior Research and Therapy, 43,* 1391-1424.

Lovell, M. R., Collins, M. W., Podell, K., Powell, J., & Maroon, J. (2000). ImPACT: Immediate post-concussion assessment and cognitive testing. Pittsburgh, PA: NeuroHealth Systems, LCC.

Lovibond, P. F., & Lovibond, S. H. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behaviour research and therapy,33(3), 335-343.

Mainwaring, L. M., Hutchison, M., Bisschop, S. M., Comper, P., & Richards, D. W. (2010). Emotional response to sport concussion compared to ACL injury. *Brain injury*, *24*(4), 589-597.

Mainwaring, L., Hutchison, M., Camper, P., & Richards, D. (2012). Examining emotional sequelae of sport concussion. *Journal of Clinical Sport Psychology*, *6*(3), 247-274.

Maren, S. (2001). Neurobiology of Pavlovian fear conditioning. *Annual Reviews of Neuroscience, 24,* 897-931.

Martin-Soelch, C., Linthicum, J., & Ernst, M. (2007). Appetitive conditioning: neural bases and implications for psychopathology. *Neuroscience & Biobehavioral Reviews*, *31*(3), 426-440.

Matsushita, M., Hosoda, K., Naitoh, Y., Yamashita, H., & Kohmura, E. (2011). Utility of diffusion tensor imaging in the acute stage of mild to moderate traumatic brain injury for detecting white matter lesions and predicting long-term cognitive function in adults: Clinical article. *Journal of Neurosurgery*, *115*(1), 130-139.

Matthews, S.C., Strigo, I.A., Simmons, N.A., O'Connell, R.M., Reinhardt, L.E., & Moseley, S.A. (2011). A multimodal imaging study in U.S. veterans of Operations Iraqi and Enduring Freedom with and without major depression after blast-related concussion. *NeuroImage, 54,* S69-S75.

McCaffrey, M.A., Mihalik, J.P., Crowell, D.H., Shields, E.W., & Guskiewicz, K.M. (2007). Measurement of head impacts in collegiate football players: Clinical measures of concussion after high- and low-magnitude impacts. *Neurosurgery, 61*(6), 1236-1243.

McCrea, M., Hammeke, T., Olsen, G., Leo, P., & Guskiewicz, K.M. (2004). Unreported concussion in high school football players: Implications for prevention. *Clinical Journal of Sports Medicine, 14*(1), 13-17.

McCrory, P., Meeuwisse, W.H., Aubry, M., Cantu, B., Dvorak, J., Echemendia, R.J., … Tuner, M. (2013). Consensus statement on concussion in sport: The 4th international conference on concussion in sport held in Zurich, November 2012.

McCrory, P., Meeuwisse, W., Dvorak, J., Aubry, M., Bailes, J., Broglio, S., ... & Davis, G. A. (2017). Consensus statement on concussion in sport—the 5th international conference on concussion in sport held in Berlin, October 2016. *Br J Sports Med*, bjsports-2017.

McKee, A.C., Cantu, R.C., Nowinski, C.J., Hedley-Whyte, E.T., Gavett, B.E., Budson, A.E., Santini, V.E., Lee, H., Kubilus, C.A., & Stern, R.A. (2009). Chronic traumatic encephalopathy in athletes: Progressive tauopathy following repetitive head injury. *Journal of Neuropathology & Clinical Neurology, 68*(7), 709-735.

Meaney, D.F. & Smith, D.H. (2011). Biomechanics of concussion. *Clinical Sports Medicine, 30,* 19-31.

Meares, S., Shores, E.A., Batchelor, J., Baguley, I.J., Chapman, J., Gurka, J., & Marosszeky, J.E. (2006). The relationship of psychological and cognitive factors and opioids in the development of the postconcussion syndrome in general trauma patients with mild traumatic brain injury. *Journal of the International Neuropsychological Society, 12,* 792-801.

Meares, S., Shores, E.A., Taylor, A.J., Batchelor, J., Bryant, R.A., Baguley, I.J., … Marossjeky, J.E. (2008). Mild traumatic brain injury does not predict acute postconcussion syndrome. *Journal of Neurology, Neurosurgery, and Psychiatry, 79*(3), 300-306.

Meares, S., Shores, E.A., Taylor, A.J., Batchelor, J., Bryant, R.A., Baguley, I.J., …, Marrosjeky, J.E. (2011). The prospective course of postconcussion syndrome: The role of mild traumatic brain injury. *Neuropsychology, 25*(4), 454-465.

Mendez, C.V., Hurley, R.A., Lassonde, M., Zhang, L., & Taber, K.H. (2005). Mild traumatic brain injury: Neuroimaging of sports-related concussion. *The Journal of Neuropsychiatry and Clinical Neurosciences, 17*(3), 297-303.

Meyer, D.L., Davies, D.R., Barr, J.L., Manzerra, P., & Forster, G.L. (2012). Mild traumatic brain injury in the rat alters neuronal number in the limbic system and increases conditioned fear and anxiety-like behaviors. *Experimental Neurology, 235,* 574-587.

Meyer, D., Leventhal, H., & Gutmann, M. (1985). Common-sense models of illness: The example of hypertension. *Health Psychology, 4,* 115-135.

Mooney, G. & Speed, J. (2001). The association between mild traumatic brain injury and psychiatric conditions. *Brain Injury, 15*(10), 865-877.

Moore, E.L., Terryberry-Spohr, L. Hope, D.A. (2006). Mild traumatic brain injury and anxiety sequelae: A review of the literature. *Brain Injury, 20*(2), 117-132.

Mora, A.G., Ritenour, A.E., Wade, C.E., Holcomb, J.B., Blackbourne, L.H., & Gaylord, K.M. (2009). Posttraumatic stress disorder in combat casualties with burns sustaining primary blast and concussive injuries. *Journal of Trauma-Injury Infection & Critical Care, 66*(4), S178-S185.

Moss-Morris, R., Petrie, K.J., & Weinman, J. (1996). Functioning in chronic fatigue syndrome: Do illness perceptions play a regulatory role? *British Journal of Health Psychology, 1,* 15-25.

Moss-Morris, R., Weinman, J., Petrie, J.K., Horne, R., Cameron, L.D., & Buick, D. (2002). The Revised Illness Perception Questionnaire (IPQ-R). *Psychology and Health, 17*(1), 1-16.

National Center for Injury Prevention and Control. Report to Congress on Mild Traumatic Brain Injury in the United States: Steps to Prevent a Serious Public Health Problem. Atlanta, GA: Centers for Disease Control and Prevention; 2003.

Nerenz, D.R. & Leventhal, H. (1983). Self-regulation theory in chronic illness. In Burish, T.G. & Bradley, L.A. (Eds.), *Coping with Chronic Disease Research and Applications* (13-37). New York: Academic Press.

Neumann, D.L. & Waters, A.M. (2006). The use of an unpleasant sound as an unconditional stimulus in a human aversive Pavlovian conditioning procedure. *Biological Psychology, 73,* 175-185.

Neumann, D.L., Waters, A.M., Westbury, H.R., & Henry, J. (2008). The use of an unpleasant sound unconditional stimulus in an aversive conditioning procedure with 8- to 11- year-old children. *Biological Psychology, 79*(3), 337-342.

Niogi, S. N., & Mukherjee, P. (2010). Diffusion tensor imaging of mild traumatic brain injury. *The Journal of Head Trauma Rehabilitation, 25*(4), 241-255.

Nutt, D. J., & Malizia, A. L. (2004). Structural and functional brain changes in posttraumatic stress disorder. *Journal of Clinical Psychiatry, 65*(1), 11-17.

Ono, K. & Kanno, M. (1996). Influences of the physical parameters on the risk to neck injuries in low impact speed rear-end collisions. *Accident Analysis and Prevention, 28,* 493-499.

Orr, S.P., Metzger, L.J., Lasko, N.B., Macklin, M.L., Peri, T., & Pitman, R.K. (2000). De novo conditioning in trauma-exposed individuals with and without posttraumatic stress disorder. *Journal of Abnormal Psychology, 109*(2), 290-298.

Ozen, L. J., & Fernandes, M. A. (2011). Effects of "diagnosis threat" on cognitive and affective functioning long after mild head injury. *Journal of the International Neuropsychological Society, 17*(02), 219-229.

Patterson, Z. R., & Holahan, M. R. (2012). Understanding the neuroinflammatory response following concussion to develop treatment strategies. *Frontiers in cellular neuroscience*, *6*.

Peri, T., Ben-Shakhar, G., Orr, S.P., & Shalev, A.Y. (2000). Psychophysiologic assessment of aversive conditioning in posttraumatic stress disorder. *Biological Psychiatry, 47*, 512-519.

Pertab, J.L., James, K.M., & Bigler, E.D. (2009). Limitations of mild traumatic brain injury meta-analyses. *Brain Injury, 23,* 498-508.

Petrie, K. J., Cameron, L. D., Ellis, C. J., Buick, D., & Weinman, J. (2002). Changing illness perceptions after myocardial infarction: an early intervention randomized controlled trial. *Psychosomatic medicine*, *64*(4), 580-586.

Potter, S., Leigh, E., Wade, D., & Fleminger, S. (2006). The Rivermead post concussion symptoms questionnaire. *Journal of Neurology*, *253*(12), 1603-1614.

Preacher, K. J., & Hayes, A. F. (2008). Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behavior Research Methods*, *40*(3), 879-891.

Quirk, G.J. & Beer, J.S. (2006). Prefrontal involvement in the regulation of emotion: Convergence of rat and human studies. *Current Opinion in Neurobiology, 16*(6), 723-727.

Quirk, G.J., Repa, J.C., LeDoux, J.E. (1995). Fear conditioning enhances short-latency auditory responses of lateral amygdala neurons: Parallel recordings in the freely behaving rat. *Neuron, 15,* 1029-1039.

Rabinowitz, A.R., Li, X., & Levin, H.S. (2014) Sport and nonsport etiologies of mild traumatic brain injury: Similarities and differences. *The Annual Review of Psychology, 65,* 301-331.

Rao, V., & Lyketsos, C. G. (2002). Psychiatric aspects of traumatic brain injury. *Psychiatric Clinics of North America, 25*(1), 43-69.

Reger, M.L., Poulos, A.M., Buen, F., Giza, C.C., Hovda, D.A., & Fanselow, M.S. (2012). Concussive brain injury enhances fear learning and excitatory processes in the amygdala. *Biological Psychiatry, 71,* 335-343.

Reiner, A., Heldt, S.A., Presley, C.S., Guley, N.H., Elberger, A.J., Deng, Y., … Moore II, B.M. (2015). Motor, visual, and emotional deficits in mice after closed-head mild traumatic brain injury are alleviated by the novel CB2 inverse agonist SMM-189. *International Journal of Molecular Sciences, 16,* 758-787.

Rimmele, U., Zellweger, B. C., Marti, B., Seiler, R., Mohiyeddini, C., Ehlert, U., & Heinrichs, M. (2007). Trained men show lower cortisol, heart rate and psychological responses to psychosocial stress compared with untrained men. Psychoneuroendocrinology, 32, 627-635.

Rimmele, U., Seiler, R., Marti, B., Wirtz, P. H., Ehlert, U., Heinrichs, M. (2009). The level of physical activity affects adrenal and cardiovascular reactivity to psychosocial stress. Psychoneuroendocrinology, 34, 190-198.

Ruff, R.M., Iverson, G.L., Barth, J.T., Bush, S.S., & Broshek, D.K. (2009). Recommendations for diagnosing a mild traumatic brain injury: A National Academy of Neuropsychology education paper. *Archives of Clinical Neuropsychology, 24*(1), 3-10.

Rutter, C. L., & Rutter, D. R. (2007). Longitudinal analysis of the illness representation model in patients with irritable bowel syndrome (IBS). *Journal of Health Psychology*, *12*(1), 141-148.

Sah, P., Faber, E.S.L., Lopez de Armentia, M., & Power, J. (2003). The amygdaloid complex: Anatomy and physiology. *Physiology Review, 83,* 803-834.

Schatz, P., Pardini, J. E., Lovell, M. R., Collins, M. W., & Podell, K. (2006). Sensitivity and specificity of the ImPACT test battery for concussion in athletes. Archives of Clinical Neuropsychology, 21, 91-99. doi: 10.1016/j.acn.2005.08.001

Schneider, K. J., Iverson, G. L., Emery, C. A., McCrory, P., Herring, S. A., & Meeuwisse, W. H. (2013). The effects of rest and treatment following sport-related concussion: a systematic review of the literature. *British Journal of Sports Medicine, 47*(5), 304-307.

Schneiderman, A., Braver, E.R., & Kang, H.K. (2008). Understanding sequelae of injury mechanisms and mild traumatic brain injury incurred during the conflicts in Iraq and Afghanistan: Persistent postconcussive symptoms and posttraumatic stress disorder. *American Journal of Epidemiology, 167,* 1446-1452.

Schoenhuber, R. & Gentilini, M. (1988). Anxiety and depression after mild head injury: A case control study. *Journal of Neurology, Neurosurgery, and Psychiatry, 51,* 722-724.

Schweckendiek, J., Klucken, T., Merz, C.J., Tabbert, K., Walter, B., Ambach, W., …, Stark, R. (2011). Weaving the (neuronal) web: fear learning in spider phobia. *Neuroimage, 54*, 681-688.

Sehlmeyer, C., Schoning, S., Zwitserlood, P., Pfleiderer, B., Kircher, T., Arolt, V., & Konrad, C. (2009). Human fear conditioning and extinction in neuroimaging: A systematic review. *Public Library of Online Science, 4*(6), e5865

Shenton, M. E., Hamoda, H. M., Schneiderman, J. S., Bouix, S., Pasternak, O., Rathi, Y., ... & Zafonte, R. (2012). A review of magnetic resonance imaging and diffusion tensor imaging findings in mild traumatic brain injury. Brain Imaging and Behavior, 6(2), 137-192.

Shin, L.M., Rauch, S.L., & Pitman, R.K. (2006). Amygdala, medial prefrontal cortex, and hippocampal function in PTSD. *Annals of the New York Academy of Science, 1071*, 67-79.

Shumyatsky, G.P., Malleret, G., Shin, R.M., Takizawa, S., Tully, K., Tsvetkoy, E., …, Bolshakov, V.Y. (2005). Stathmin, a gene enriched in the amygdala, controls both learned and innate fear. *Cell, 123*(4), 697-709.

Silverberg, N.D. & Iverson, G.L. (2011). Etiology of the post-concussion syndrome: Physiogenesis and psychogenesis revisited. *NeuroRehabilitation, 29*, 317-329.

Simmons, A.N. & Matthews, S.C. (2012). Neural circuitry of PTSD with or without mild traumatic brain injury: A meta-analysis. *Neuropharmacology, 62*, 598-606.

Skinner, C.T. & Hampson, S.E. (1998). Social support and personal models of diabetes in relation to self-care and well-being in adolescents with type I diabetes mellitus. *Journal of Adolescence, 21*, 61-70.

Smith, M.E. (2005). Bilateral hippocampal volume reduction in adults with post-traumatic stress disorder: A meta-analysis of structural MRI studies. *Hippocampus, 15*(6), 798-807.

Smith, S. M., & Vale, W. W. (2006). The role of the hypothalamic-pituitary-adrenal axis in neuroendocrine responses to stress. *Dialogues in clinical neuroscience, 8*(4), 383.

Snell, D.L., Hay-Smith, E.J.C., Surgenor, L.J., & Siegert, R.J. (2013). Examination of oucome after mild traumatic brain injury: The contribution of injury beliefs and Leventhal's common sense model. *Neuropsychological Rehabilitation, 23*(3), 333-362.

Snell, D.L., Siegert, R.J., Hay-Smith, E.J.C., & Surgenor, L.J. (2011a). Associations between illness perceptions, coping styles and outcome after mild traumatic brain injury: Prelimary results from a cohort study. *Brain Injury, 25*(11), 1126-1138.

Snell, D.L., Siegert, R.J., Hay-Smith, E.J.C., & Surgenor, L.J. (2011b). Factor structure of the brief COPE in people with mild traumatic brain injury. *Journal of Head Trauma Rehabilitation, 26*(6), 468-477.

Somers, J.M., Goldner, E.M., Waraich, P., & Hsu, L. (2006). Prevalence and incidence studies of anxiety disorders: A systematic review of the literature. *Canadian Journal of Psychiatry, 51*, 100-113.

Steimer, T. (2002). The biology of fear – and anxiety – related behaviors. *Dialogues in Clinical Neuroscience, 4*(3), 231-249.

Stein, M.B. & McAllister, T.W. (2009). Exploring the convergence of posttraumatic stress disorder and mild traumatic brain injury. *American Journal of Psychiatry, 166,* 768-776.

Stein, M.B., Simmons, A.N., Feinstein, J.S., & Paulus, M.P. (2007). Increased amygdala and insula activation during emotion processing in anxiety-prone subjects. *American Journal of Psychiatry, 164,* 318-327.

Stulemeijer, M., van der Werf, S., Borm, G.F., & Vos, P.E. (2008). Early prediction of favourable recovery 6 months after mild traumatic brain injury. *Journal of Neurology, Neurosurgery, and Psychiatry, 79*(8), 936-942.

Suhr, J. A., & Gunstad, J. (2002). "Diagnosis threat": The effect of negative expectations on cognitive performance in head injury. *Journal of Clinical and Experimental Neuropsychology, 24*(4), 448-457.

Terrio, H., Brenner, L.A., Ivins, B.J., Cho, J.M., Helmick, K., Schwab, K., … Warden, D. (2009). Traumatic brain injury screening: Preliminary findings in a US army bridge combat team. *Journal of Head Trauma Rehabilitation, 24,* 14-23.

Thurman, D.J. The epidemiology and economics of head trauma. In: Miller L, Hayes R, editors. Head Trauma: Basic, Preclinical, and Clinical Directions. New York: John Wiley and Sons; 2001. Thurman, D.J., Branche, C.M., & Sniezek, J.E. (1998). The epidemiology of sports-related traumatic brain injuries in the United States: Recent developments. *Journal of Head Trauma Rehabilitation, 13*(2), 1-8.

Tomberg, T., Toomela, A., Pulver, A., and Tikk, A. (2005). Coping strategies, social support, life orientation and health-related quality of life following traumatic brain injury. *Brain Injury, 19*(14), 1181-1190.

Van Wilgen, C.P., Kaptein, A.A., & Brink, M.S. (2010). Illness perceptions and mood states are associated with injury-related outcomes in athletes. *Disability and Rehabilitation, 32*(19), 1576-1585.

Vaschillo, B., Vaschillo, A.G., McLaughlin, J., Vickroy, M., Bergen, M.T., & Servatius, R.J. (2003). Aversive quality of sounds: Psychophysiological characteristics. *Pychophysiology, 40,* S87.

Vaschillo, E.G., Vaschillo, B., Bergen, M.T., McLaughlin, & Servatius, R.J. (2003). Aversive quality of sounds: Role of infrasonic components. *Pychophysiology, 40,* S87.

Vasterling. J.J., Verfaellie, M., Sullivan, K.D. (2009). Mild traumatic brain injury and posttraumatic stress disorder in returning veterans: Perspectives from cognitive neuroscience. *Clinical Psychology Review, 29,* 674-684.

Verner, M., Conzelmann, A., Lehnert, K., Seiler, R., Wassmer, A., & Rammsayer, T. (2010). Subjective stress in female elite athletes and non-athletes: Evidence from cortisol analyses. *Europe's journal of psychology*, *6*(4), 56-70.

Viano, D.C., Casson, I.R., Pellman, E.J., Zhang, L., King, A.I., & Yang, K.H. (2005). Concussion in professional football: Brain responses by finite element analysis: Part 9. *Neurosurgery, 57,* 891-916.

Vreeburg, S. A., Zitman, F. G., van Pelt, J., DeRijk, R. H., Verhagen, J. C., van Dyck, R., ... & Penninx, B. W. (2010). Salivary cortisol levels in persons with and without different anxiety disorders. *Psychosomatic medicine*, *72*(4), 340-347.

Vreeburg, S. A., Hoogendijk, W. J., DeRijk, R. H., van Dyck, R., Smit, J. H., Zitman, F. G., & Penninx, B. W. (2013). Salivary cortisol levels and the 2-year course of depressive and anxiety disorders. *Psychoneuroendocrinology*, *38*(9), 1494-1502.

Walilko, T., North, C., Young, L.A., Lux, W.E., Warden, D.L., Jaffee, M.S., & Moore, D.F. (2009). Head injury as a PTSD predictor among Oklahoma City bombing survivors. *Journal of Trauma*, *67*(6), 1311-1319.

Watson, J. B., & Rayner, R. (1920). Conditioned emotional reactions. *Journal of Experimental Psychology, 3,* 1–14.

Weinman, J., Petrie, K.J., Moss-Morris, R., & Horne, R. (1996). The Illness Perception Questionnaire: A new method for assessing illness perceptions. *Psychology and Health, 11*, 431-446.

Weisenkrantz, L. (1956). Behavioral changes associated with ablations of the amygdaloid complex in monkeys. *Journal of Comparative and Physiological Psychology, 49*, 381-391.

Whittaker, R., Kemp, S., & House, A. (2007). Illness perceptions and outcome in mild head injury: A longitudinal study. *Journal of Neurology, Neurosurgery, & Psychiatry, 78*, 644-646.

Williamson, J.B., Heilman, K.M., Porges, E.C., Lamb, D.G., & Porges, S.W. (2013). A possible mechanism for PTSD symptoms in patients with traumatic brain injury: Central autonomic network disruption. *Frontiers in Neuroengineering, 6*(13). Advance online publication doi: 10.3389/fneng.2013.00013

Wong, D., Dahm, J., & Ponsford, J. (2013). Factor structure of the Depression Anxiety Stress Scales in individuals with traumatic brain injury. Brain injury,27(12), 1377-1382.

Wood, R.L. (2004). Understanding the 'miserable minority': a diathesis-stress paradigm for post-concussional syndrome. *Brain Injury, 18*(11), 1135-115.

Woodrome, S.E., Yeates, K.O., Taylor, H.G., Rusin, J., Bangert, B., Dietrich, A., …, Wright, M. (2011). Coping strategies as a predictor of post-concussive symptoms in children with mild traumatic brain injury versus mild orthopedic injury. *Journal of the International Neuropsychological Society, 17*(2), 317-326.

Yoshino, A., Hovda, D.A., Kawamata, T., & Becker, D.P. (1991). Dynamic changes in local cerebral glucose utilization following cerebral contusion in rats: Evidence of a hyper- and subsequent hypometabolic state. *Brain Research, 561,* 106-119.

Zetterberg, H., Hietala, M.A., Jonsson, M., Andreasen, N., Styrud, E., Karlsson, I., …, Wallin, A. (2006). Neurochemical aftermath of amateur boxing. *Archives of Neurology, 63*(9), 1277-1280.

Zhang, L., Hier, L.A., Zimmerman, R.D., Jordan, B.D., & Ulug, A.M. (2006). Diffusion anisotropy changes in brains of professional boxers. *American Journal of Neuroradiology, 27*(9), 2000-2004.

APPENDIX A
Intake Interview Form

U WINDSOR: SPORTS CONCUSSION CLINIC

INTAKE EVALUATION FORM

First name: _____

Surname: _____

Interviewer: _____

Date of Interview: _____ _____ _____ _____ _____ _____ _____ _____
M M D D Y Y Y Y

Participant Group: ☐ Not participating in reseach
☐ Referred to concussion clinic
☐ Referred from undergrduate participant pool

Participant ID: _____

Section I: Demographics

Date of Birth: ☐☐☐☐☐☐☐☐ (M M D D Y Y Y Y)

Dominant Hand:
- ☐ Right
- ☐ Left
- ☐ Ambidextrous

Primary (native) language: ☐

Secondary language(s): ☐

Country of birth: ☐

Prompt: What is your gender?

Gender:
- ☐ Male
- ☐ Female
- ☐ Other

Marital status: (check one)
- ☐ Single, never married
- ☐ In relationship, not married
- ☐ Married
- ☐ Separated
- ☐ Divorced
- ☐ Widowed
- ☐ Other

Ethnicity: ☐

Living Situation:
- ☐ In parents home
- ☐ Alone
- ☐ With roommates
- ☐ In residence
- ☐ With partner
- ☐ Other

Section II: Education

How many years of post-secondary education have you **completed?**

- ☐ 1
- ☐ 2
- ☐ 3
- ☐ 4
- ☐ 5
- ☐ 6+

What is your major? ☐

Are you a full time or part-time student?

- ☐ Full time
- ☐ Part-time

Having you ever been diagnosed with any of the following:

☐ ADHD
☐ Learning disability

When were you diagnosed and by whom?

Have you ever received extra assistance in school (e.g., IEP, modified curriculum, allowed extra time)?

☐ Yes
☐ No

Describe:

Aside from being a student, are you currently working?

☐ Yes, full time
☐ Yes, part time
☐ No

Describe:

***** SKIP SECTION V for CONTROLS *****

Section III: Current Concussion

When was your most recent injury (date)?

M	M	D	D	Y	Y	Y	Y

How did it happen?

What did you experience directly after the injury? (approx the following 24 hours)

Loss of consciousness	☐ Yes	☐ No
Feeling confused	☐ Yes	☐ No
Loss of memory for things that happened directly after the injury	☐ Yes	☐ No
Loss of memory for things that happened directly before the injury	☐ Yes	☐ No

Describe:

Did you receive medical treatment? ☐ Yes ☐ No

Describe:

What have you been doing since the injury?

Physical activities ☐ Yes ☐ No Describe:

Cognitive activities ☐ Yes ☐ No Describe:

Change in concentration ☐ Yes ☐ No Describe:

Stressors ☐ Yes ☐ No Describe:

Rate your level of distress on a scale from 0-9: ☐

Change in appetite ☐ Yes ☐ No Describe:

Change in sleep ☐ Yes ☐ No Describe:

Section IV: Medical/Psychiatric

Current medical problems and services received(ing) for them (e.g., medications, treatment):
(other than recent head injury/concussion)

Condition 1:

Received(ing) treatment: ☐ Yes ☐ No

Describe treatment

Medication(s)

Condition 2:

Received(ing) treatment: ☐ Yes ☐ No

Describe treatment

Medication(s)

Condition 3:

Received(ing) treatment: ☐ Yes ☐ No

Describe treatment

Medication(s)

Are you currently taking any medications including over the counter medications? Please list:

Past medical problems and services received for them (e.g., medications, treatment):

Prompt: ***Are you currently experiencing any pain (in the past 7 days)?***

☐ Yes ☐ No

Rating of most severe location:
0=none 4=moderate
2=slight 7=significant
9=severe

Prompt: Have you ever been diagnosed or sought treatment for any of the following:

Depression:	☐	Never	☐	Past	☐	Present	Desc:
Anxiety:	☐	Never	☐	Past	☐	Present	Desc:
Bi-polar Disorder:	☐	Never	☐	Past	☐	Present	Desc:
Psychosis: (e.g., Schizophrenia)	☐	Never	☐	Past	☐	Present	Desc:
Thoughts of hurting yourself:	☐	Never	☐	Past	☐	Present	Desc:

If Yes: ***Do you have a specific plan? Access to means?***
Do you intend on following through?
Do you have support systems?
Do you feel hopeless about the future?

Prompt: Do you currently use any of the following substances:

Substance use:					
	Alcohol	☐	Never	☐	Present
	Drugs	☐	Never	☐	Present
	Tobacco	☐	Never	☐	Present

Prompt: if yes to substance use; identify how much and how often.

Section V: Athletic History

What sports team(s) are you currently a member of or have been in the past 10 years:

								# of Years
☐	Football	☐	Collegiate Varsity	☐	High-school	☐	Recreational	
☐	Soccer	☐	Collegiate Varsity	☐	High-school	☐	Recreational	
☐	Baseball/softball	☐	Collegiate Varsity	☐	High-school	☐	Recreational	
☐	Hockey	☐	Collegiate Varsity	☐	High-school	☐	Recreational	
☐	Basketball	☐	Collegiate Varsity	☐	High-school	☐	Recreational	
☐	Tennis	☐	Collegiate Varsity	☐	High-school	☐	Recreational	
☐	Other	☐	Collegiate Varsity	☐	High-school	☐	Recreational	

Ask only if participant is not on a varsity team:

What kind of exercise do you do and how often?

Section VI: Physiological Status

How many hours of sleep did you get last night?

	In the last 24 hours:		*Since the concussion:*	
Did you do any physical activity?	☐ Yes ☐ No		☐ Yes ☐ No	Describe:
Did you take any medications? *(prescription, over-the counter, illegal)*	☐ Yes ☐ No		☐ Yes ☐ No	Describe (name and dosage)

Did you drink any alcohol?	☐ Yes ☐ No	☐ Yes ☐ No	Describe (how many and what kind)	
Did you drink any caffeinted beverages? *(coffee, tea, energy drink, soda/pop)*	☐ Yes ☐ No	☐ Yes ☐ No	Describe (how many and what kind)	

Prompt: As part of this research study we may want to contact you regarding some follow-up information. Would it be alright contact you at a later date (in 3-6 months) regarding more research?

☐ No ☐ Yes If Yes: Telephone: H | | | | | | | | | | |
M | | | | | | | | | | |

Email:

Section VII: Brain Injury Symptom Questionnaire (BISQ)

Administer BISQ

******TO COMPLETE FOLLOWING INTERVIEW******

CURRENT MENTAL STATUS

Appearance:	☐ well-groomed	☐ disheveled	☐ bizarre	☐ inappropriate	
Attitude:	☐ cooperative	☐ guarded	☐ suspicious	☐ uncooperative	☐ belligerent
Motor Activity:	☐ calm	☐ hyperactive	☐ agitated	☐ tremors/tics	☐ muscle spasm
Affect:	☐ appropriate	☐ labile	☐ expansive	☐ constricted/flat	☐ blunted
Mood:	☐ calm	☐ depressed	☐ anxious	☐ angry	☐ euphoric
Speech:	☐ normal	☐ delayed ☐ pressured	☐ soft ☐ loud	☐ slurred ☐ excessive	☐ incoherent ☐ perserverating
Thot. Process:	☐ normal	☐ circumstantial	☐ loose assoc.	☐ tangential	☐ flight of ideas
Thot. Content:	☐ normal	hallucinations: delusions:	☐ auditory ☐ persecutory	☐ visual ☐ being contrld	☐ olfactory ☐ thought insert. ☐ bizarre
Self-Perception:	☐ normal	☐ depersonalizn.	☐ derealization		
Orientation:	☐ normal	☐ disoriented:	☐ time	☐ place	☐ person
Memory:	☐ intact	☐ impaired:	☐ immediate	☐ recent amnes: amnesia	☐ remote
Judgement:	☐ intact	☐ impaired:	☐ minimal	☐ moderate	☐ severe
Insight:	☐ intact	☐ impaired	☐ minimal	☐ moderate	☐ severe
Risk Factors:	☐ none reported	☐ suicidality ☐ alcohol abuse	☐ homicidality ☐ substance abuse	☐ medical risk ☐ victim of abuse	☐ impulse control ☐ perpetrator of abuse

APPENDIX B
Brain Injury Screening Questionnaire –Adapted (BISQ-A)

Brain Injury Screening Questionnaire – Adapted for SCC										Version 7.8.2012
Column A		Column B								
For each event listed, record the number of times you have ever experienced the following situations..		Ever lose consciousness?		Ever dazed and confused?		Posttraumatic Amnesia?		Retrograde Amnesia?		
	How many times?	How many times?	Longest period?	How many times?	Longest period?	How many times?	Longest period?	How many times?	Longest period?	
1. In a motor vehicle crash (e.g., car, motorcycle)?										
2. A pedestrian hit by a vehicle?										
3. Running into or being hit by an object (e.g., equipment)?										
4. Falling, fainting or slipping?										
5. During a drug or alcohol blackout?										
6. While biking?										
7. While roller balding/skateboarding?										
8. While horseback riding?										
9. While skiing/snowboarding?										

10. In sports (football, baseball basketball)?									
11. While on the playground?									
12. While diving into water?									
13. Being assaulted or mugged?									
14. Being physically abused?									
15. Other?									

Ever been hospitalized or seen in the emergency room for any of the following?		Ever lose consciousness?		Ever dazed and confused?		Posttraumatic Amnesia?		Retrograde Amnesia?	
	How many times?	How many times?	Longest period?	How many times?	Longest period?	How many times?	Longest period?	How many times?	Longest period?
1. Concussion?									
2. Fracture to the head, neck or face?									
3. Seizures?									
4. High fever?									
5. Near drowning?									
6. Poisoning?									
7. Hit by lightening?									
8. Electrical power injury?									
9. Gun shot injury?									

10. Stroke/brain hemorrhage?									
11. Brain infection?									
12. Other injury?									

APPENDIX C
Depression, Anxiety, and Stress Scale (DASS)

DASS

Name: *Date:*

Please read each statement and circle a number 0, 1, 2 or 3 that indicates how much the statement applied to you *over the past week*. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 Did not apply to me at all
1 Applied to me to some degree, or some of the time
2 Applied to me to a considerable degree, or a good part of time
3 Applied to me very much, or most of the time

1	I found myself getting upset by quite trivial things	0	1	2	3
2	I was aware of dryness of my mouth	0	1	2	3
3	I couldn't seem to experience any positive feeling at all	0	1	2	3
4	I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)	0	1	2	3
5	I just couldn't seem to get going	0	1	2	3
6	I tended to over-react to situations	0	1	2	3
7	I had a feeling of shakiness (eg, legs going to give way)	0	1	2	3
8	I found it difficult to relax	0	1	2	3
9	I found myself in situations that made me so anxious I was most relieved when they ended	0	1	2	3
10	I felt that I had nothing to look forward to	0	1	2	3
11	I found myself getting upset rather easily	0	1	2	3
12	I felt that I was using a lot of nervous energy	0	1	2	3
13	I felt sad and depressed	0	1	2	3
14	I found myself getting impatient when I was delayed in any way (eg, elevators, traffic lights, being kept waiting)	0	1	2	3
15	I had a feeling of faintness	0	1	2	3
16	I felt that I had lost interest in just about everything	0	1	2	3
17	I felt I wasn't worth much as a person	0	1	2	3

18	I felt that I was rather touchy	0	1	2	3
19	I perspired noticeably (eg, hands sweaty) in the absence of high temperatures or physical exertion	0	1	2	3
20	I felt scared without any good reason	0	1	2	3
21	I felt that life wasn't worthwhile	0	1	2	3

Please turn the page ☞

Reminder of rating scale:

0 Did not apply to me at all
1 Applied to me to some degree, or some of the time
2 Applied to me to a considerable degree, or a good part of time
3 Applied to me very much, or most of the time

22	I found it hard to wind down	0	1	2	3
23	I had difficulty in swallowing	0	1	2	3
24	I couldn't seem to get any enjoyment out of the things I did	0	1	2	3
25	I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)	0	1	2	3
26	I felt down-hearted and blue	0	1	2	3
27	I found that I was very irritable	0	1	2	3
28	I felt I was close to panic	0	1	2	3
29	I found it hard to calm down after something upset me	0	1	2	3
30	I feared that I would be "thrown" by some trivial but unfamiliar task	0	1	2	3
31	I was unable to become enthusiastic about anything	0	1	2	3
32	I found it difficult to tolerate interruptions to what I was doing	0	1	2	3
33	I was in a state of nervous tension	0	1	2	3
34	I felt I was pretty worthless	0	1	2	3
35	I was intolerant of anything that kept me from getting on with what I was doing	0	1	2	3
36	I felt terrified	0	1	2	3
37	I could see nothing in the future to be hopeful about	0	1	2	3
38	I felt that life was meaningless	0	1	2	3

39	I found myself getting agitated	0	1	2	3
40	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3
41	I experienced trembling (eg, in the hands)	0	1	2	3
42	I found it difficult to work up the initiative to do things	0	1	2	3

Scoring:

Scores of Depression, Anxiety and Stress are calculated by summing the scores for the relevant items. The depression scale items are 3, 5, 10, 13, 16, 17, 21, 24, 26, 31, 34, 37, 38, 42. The anxiety scale items are 2, 4, 7, 9, 15, 19, 20, 23, 25, 28, 30, 36, 40, 41. The stress scale items are 1, 6, 8, 11, 12, 14, 18, 22, 27, 29, 32, 33, 35, 39. To use the Scoring Template (below) print on to a plastic overhead. The score for each of the respondents over each of the sub-scales, are then evaluated as per the severity-rating index below.

	Depression	Anxiety	Stress
Normal	0 – 9	0 - 7	0 – 14
Mild	10 – 13	8 – 9	15 – 18
Moderate	14 – 20	10 – 14	19 – 25
Severe	21 – 27	15 – 19	26 – 33
Extremely Severe	28+	20+	34 +

Norms: Normative data are available on a number of Australian samples. From a sample of 2914 adults the means (and standard deviations) were 6.34 (6.97), 4.7 (4.91), and 10.11 (7.91) for the depression, anxiety, and stress scales, respectively. A clincical sample reported means (and standard deviations) of 10.65 (9.3), 10.90 (8.12), and 21.1 (11.15) for the three measures.

APPENDIX D
Post-Concussion Symptom Scale (PCSS)

Complete the following questionnaire about yourself.

Please indicate the level for which you are currently experiencing the following symptoms. If you are not currently experiencing the particular symptom, please check the box indicating "not experiencing".

Symptom	Not Experien-cing	Minor		Moderate		Severe	
Headache		1	2	3	4	5	6
Nausea		1	2	3	4	5	6
Vomiting		1	2	3	4	5	6
Balance Problems		1	2	3	4	5	6
Dizziness		1	2	3	4	5	6
Fatigue		1	2	3	4	5	6
Trouble Falling Asleep		1	2	3	4	5	6
Sleeping More Than Usual		1	2	3	4	5	6
Sleeping Less Than Usual		1	2	3	4	5	6
Drowsiness		1	2	3	4	5	6
Sensitivity to Light		1	2	3	4	5	6
Sensitivity to Noise		1	2	3	4	5	6
Irritability		1	2	3	4	5	6
Sadness		1	2	3	4	5	6
Nervousness		1	2	3	4	5	6
Feeling More Emotional		1	2	3	4	5	6
Numbness or Tingling		1	2	3	4	5	6
Feeling Slowed Down		1	2	3	4	5	6
Feeling Mentally "Foggy"		1	2	3	4	5	6
Difficulty Concentrating		1	2	3	4	5	6

Difficulty Remembering		1	2	3	4	5	6
Visual Problems		1	2	3	4	5	6

APPENDIX E

Brief COPE

These items deal with ways you've been coping with the stress in your life. There are many ways to try to deal with problems. These items ask what you've been doing to cope with this one. Obviously, different people deal with things in different ways, but I'm interested in how you've tried to deal with it. Each item says something about a particular way of coping. I want to know to what extent you've been doing what the item says. How much or how frequently. Don't answer on the basis of whether it seems to be working or not—just whether or not you're doing it. Use these response choices. Try to rate each item separately in your mind from the others. Make your answers as true FOR YOU as you can.

1 = I haven't been doing this at all
2 = I've been doing this a little bit
3 = I've been doing this a medium amount
4 = I've been doing this a lot

1. I've been turning to work or other activities to take my mind off things.
2. I've been concentrating my efforts on doing something about the situation I'm in.
3. I've been saying to myself "this isn't real.".
4. I've been using alcohol or other drugs to make myself feel better.
5. I've been getting emotional support from others.
6. I've been giving up trying to deal with it.
7. I've been taking action to try to make the situation better.
8. I've been refusing to believe that it has happened.
9. I've been saying things to let my unpleasant feelings escape.
10. I've been getting help and advice from other people.
11. I've been using alcohol or other drugs to help me get through it.
12. I've been trying to see it in a different light, to make it seem more positive.
13. I've been criticizing myself.
14. I've been trying to come up with a strategy about what to do.
15. I've been getting comfort and understanding from someone.
16. I've been giving up the attempt to cope.
17. I've been looking for something good in what is happening.
18. I've been making jokes about it.
19. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping.
20. I've been accepting the reality of the fact that it has happened.

21. I've been expressing my negative feelings.
22. I've been trying to find comfort in my religion or spiritual beliefs.
23. I’ve been trying to get advice or help from other people about what to do.
24. I've been learning to live with it.
25. I've been thinking hard about what steps to take.
26. I’ve been blaming myself for things that happened.
27. I've been praying or meditating.
28. I've been making fun of the situation.

APPENDIX F
Illness Perception Questionnaire - Revised (IPQ-R)

Name…… ***Date……***

YOUR VIEWS ABOUT YOUR HEAD INJURY

Listed below are a number of symptoms that you may or may not have experienced since your head injury. Please indicate by circling *Yes* or *No*, whether you have experienced any of these symptoms since your head injury, and whether you believe that these symptoms are related to your head injury.

	I have experienced this symptom *since my head injury*		This symptom is *related to my head injury*	
Pain	**Yes**	**No**	**Yes**	**No**
Sore Throat	**Yes**	**No**	**Yes**	**No**
Nausea	**Yes**	**No**	**Yes**	**No**
Breathlessness	**Yes**	**No**	**Yes**	**No**
Weight Loss	**Yes**	**No**	**Yes**	**No**
Fatigue	**Yes**	**No**	**Yes**	**No**
Stiff Joints	**Yes**	**No**	**Yes**	**No**
Sore Eyes	**Yes**	**No**	**Yes**	**No**
Wheeziness	**Yes**	**No**	**Yes**	**No**
Headaches	**Yes**	**No**	**Yes**	**No**
Upset Stomach	**Yes**	**No**	**Yes**	**No**
Sleep Difficulties	**Yes**	**No**	**Yes**	**No**
Dizziness	**Yes**	**No**	**Yes**	**No**
Loss of Strength	**Yes**	**No**	**Yes**	**No**
Memory Problems	**Yes**	**No**	**Yes**	**No**
Concentration Problems	**Yes**	**No**	**Yes**	**No**
Irritability	**Yes**	**No**	**Yes**	**No**
Balance Problems	**Yes**	**No**	**Yes**	**No**

We are interested in your own personal views of how you now see your current head injury. Please indicate how much you agree or disagree with the following statements about your head injury by ticking the appropriate box.

VIEWS ABOUT YOUR HEAD INJURY	Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
My head injury will last a short time					
My head injury is likely to be permanent rather than temporary					

My head injury will last for a long time					
This head injury will pass quickly					
I expect to have this head injury for the rest of my life					
My head injury is a serious condition					
My head injury has major consequences on my life					
My head injury does not have much effect on my life					
My head injury strongly affects the way others see me					
My head injury has serious financial consequences					
My head injury causes difficulties for those who are close to me					
There is a lot which I can do to control my symptoms					
What I do can determine whether my head injury gets better or worse					
The course of my head injury depends on me					
Nothing I do will affect my head injury					
I have the power to influence my head injury					
My actions will have no affect on the outcome of my head injury					
My head injury will improve in time					
There is very little that can be done to improve my head injury					
My treatment will be effective in curing my head injury					
The negative effects of my head injury can be prevented (avoided) by my treatment					
My treatment can control my head injury					
There is nothing which can help my condition					

The symptoms of my condition are puzzling to me					
My head injury is a mystery to me					
I don't understand my head injury					
My head injury doesn't make any sense to me					
I have a clear picture or understanding of my condition					
The symptoms of my head injury change a great deal from day to day					
My symptoms come and go in cycles					
My head injury is very unpredictable					
I go through cycles in which my head injury gets better and worse					
I get depressed when I think about my head injury					
When I think about my head injury I get upset					
My head injury makes me feel angry					
My head injury does not worry me					
Having this head injury makes me feel anxious					
My head injury makes me feel afraid					

CAUSES OF MY HEAD INJURY

We are interested in what you consider may have been the cause of <u>your</u> head injury. As people are very different, there is no correct answer for this question. We are most interested in your own views about the factors that caused your head injury rather than what others including doctors or family may have suggested to you. Below is a list of possible causes for your head injury. Please indicate how much you agree or disagree that they were causes for you by ticking the appropriate box.

POSSIBLE CAUSES	Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
Stress or worry					

Hereditary - it runs in my family					
A Germ or virus					
Diet or eating habits					
Chance or bad luck					
Poor medical care in my past					
Pollution in the environment					
My own behaviour					
My mental attitude e.g. thinking about life negatively					
Family problems or worries caused my head injury					
Overwork					
My emotional state e.g. feeling down, lonely, anxious, empty					
Ageing					
Alcohol					
Smoking					
Accident or injury					
My personality					
Altered immunity					

In the table below, please list in rank-order the three most important factors that you now believe caused YOUR head injury. You may use any of the items from the box above, or you may have additional ideas of your own.
The most important causes for me:
1. _____
2. _____
3. _____

VITA AUCTORIS

NAME:	Sabrina Freund
PLACE OF BIRTH:	Dachau, Germany
YEAR OF BIRTH:	1987
EDUCATION:	University of Windsor, B.A. (Hons.), Windsor, Ontario, 2005-2009
	University of Windsor, M.A., Windsor, Ontario, 2010-2012
	University of Windsor, Ph.D., Windsor, Ontario, 2012-2017