

Do Sub-Concussive Impacts from Soccer Heading in Practice Cause Changes in Brain
Structure and Function?

by

Rebecca Kenny
Bachelor of Science (Hons), University of Oregon, 2014

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of the Requirements for the Degree of

Master of Science

in the School of Exercise Science, Physical and Health Education, the Division of Medical
Sciences and Psychology

Rebecca Kenny, 2018
University of Victoria

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Supervisory Committee

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Abstract

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Background: Heading is an important part of soccer, yet recent research has indicated that cumulative effects of repetitive heading may cause sub-concussive injury (Koerte et al., 2015). **Objective:** The current study aimed to prospectively investigate the effects of repetitive, intentional heading in soccer practice on brain structure and cognitive function using a within-subjects design. **Methods:** Participants included 11 soccer players ($M=20.09$, $SD=2.88$) that were examined immediately pre and post heading practice. Magnetic resonance imaging data were acquired on a 3T GE Scanner with diffusion tensor imaging (DTI). Behavioural measures were also completed pre and post soccer heading and included the Sideline Concussion Assessment Tool 3 (SCAT-3) and several short-computerized executive function tasks. An accelerometer was used to measure the force of the impact during soccer heading. Heart-rate data was collected on Polar Monitors. DTI analyses were completed using FSL's Tract Based Spatial Statistics to examine changes in both fractional anisotropy (FA) and mean diffusivity (MD) due to heading the soccer ball. The current study investigated microstructural changes and behavioural performance in young soccer players. Heart rate variability data were not available for analyses due to technical difficulties. **Results:** Heading impacts were not greater than 10g. At this level of impact, there were no significant pre-post heading differences in either FA or MD. There were no significant differences between pre and post heading in the three behavioural tasks. Additionally, there were no

significant differences in SCAT-3 scores between groups. Some practice effects were demonstrated in one behavioural task and a section of the SCAT-3. **Conclusion:** The current work shows initial evidence that repetitive heading in soccer in a practice setting does not cause changes in brain structure or cognitive function. Future research should investigate heading in games and sex differences with a greater sample size.

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Dedication

“All that I am or ever hope to be, I owe to my angel mother.”

—Abraham Lincoln

Chapter One: Introduction

Soccer is one of the most watched and most played sports, with more than 265 million people playing soccer worldwide, and upwards of 22 million youth involved in the game (FIFA Big Count, 2006). The FIFA World Cup 2014 in Brazil reached just over three billion viewers, which is indicative of the popularity of the game worldwide (FIFA Media Release, 2015). Furthermore, it's not just the men's game that draws players and viewers; the FIFA Women's World Cup 2015 in Canada drew a record breaking 750 million viewers (FIFA Media Release, 2015) and as of 2006, 26 million women play the game worldwide. In North America, there are approximately 27 million players (FIFA Big Count, 2006).

Soccer is a contact sport. Given the nature of the sport, soccer players are susceptible to numerous injuries. In past epidemiological studies, the focus has been on muscular and ligament strains and ruptures as the most common form of injuries in male English professional soccer players (Hawkins, Hulse, Wilkinson, Hodson, & Gibson, 2001). However, in recent years there has been more focus on head and neck injuries. A prospective study evaluating the incidence and causes of head and neck injuries was undertaken and determined the most common injuries were contusions, lacerations and concussions (Fuller, Junge, & Dvorak, 2005). Sport concussions are seen as a significant issue for modern athletes due to the potential long-term neurological effects (Solomon, 2018).

1.1 What is a Concussion?

Concussions are not like other forms of injuries. Usually, there are no obvious physical signs, such as swelling or bleeding, associated with concussions, and often the injured athlete appears uninjured until an evaluation of neurological symptoms is done. According to the fifth International Conference on Concussion in Sport, a sports-related concussion (SRC) is "*a traumatic brain injury induced by biomechanical forces*" (McCroory et al., 2017). An SRC may cause pathophysiological changes to the brain

and neurological impairment. Specifically, there are several common features that are used clinically to define the nature of a concussion, as reported by the Concussion in Sport Group:

- *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.*

TABLE 1 CLINICAL DOMAINS FOR CONCUSSION DIAGNOSIS (MCCRORY ET AL., 2017)

Symptoms:	
- Somatic	i.e. headache
- Cognitive	i.e. feeling like in a fog
- Emotional	i.e. mood changes
Physical signs	i.e. loss of consciousness, amnesia
Balance impairment	i.e. changes in gait
Behavioural changes	i.e. irritability
Cognitive impairment	i.e. changes in reaction times
Sleep disturbances	i.e. drowsiness

In soccer, the mechanism of a concussion among players varies and includes head on player (40% - including head to head, head to arm, and head to leg), head on ball (12.6%), and head to ground or to goalpost (10.3%) with about a third of injuries not specified (Boden, Kirkendall, & Garrett, 1998).

Additionally, upon footage review by a panel of referees, it was found that more than half of head

injuries occur during legal play (Fuller, Junge, & Dvorak, 2004), which suggests that stricter rule enforcement may not be a solution.

While sports-related concussions are a concern in soccer, it should be noted that soccer players do not suffer the most concussions when compared to other high-intensity sports like hockey, rugby and American football, both in youth and adult participation (Daneshvar, Nowinski, McKee, & Cantu, 2011; Marar, McIlvain, Fields, & Comstock, 2012; Zuckerman et al., 2015). However, one growing area of concern in soccer is that the repeated impacts to the head through heading the ball may have a cumulative effect and produce long term neurological damage. In 2002, there was significant press coverage when a coroner ruled the cause of death of Jeff Astle, a former English international football player, to be the result of his career as a soccer player and suggested that Astle's dementia was consistent with heading the ball during his career (Britten, 2002). It was noted that the front of Astle's brain showed "shrinkage and softening" and the trauma to the brain was consistent with that of boxers. Importantly, boxers were the first athletic population to be diagnosed with chronic traumatic encephalopathy (CTE), otherwise known as dementia pugilistica, due to repetitive, traumatic head impacts (Galgano, Cantu, & Chin, 2016; Koerte, Lin, Willems, et al., 2015; McKee et al., 2009; Mendez, 1995). CTE is a degenerative brain disease, caused by repeated head trauma, that results in the atrophy of brain tissue (Omalu, 2014). While the diagnosis suggests heading as a cause of death, there has not been enough evidence separating heading from other head impacts in soccer, nor have there been any studies showing a causal link between heading and any form of neurological damage.

Chapter Two: Literature Review

To understand the variability of concussions, there are issues and situations that need to be explained. The following section will clarify the differences between sub-concussive impacts and concussions, providing a framework for the current study.

2.1 Definition of a Sub-Concussive Impact

Sub-concussive impacts can be defined as blows to the head that do not cause typical concussion symptoms or result in a diagnosed concussion (Bailes, Petraglia, Omalu, Nauman, & Talavage, 2013). Sub-concussive effects may also occur with rapid-acceleration-deceleration of the body and torso causing the brain to move within the cranium (Smith et al., 2012). The key part of any definition of sub-concussive impacts is that there are no immediate symptoms reported and no outward signs of neurological dysfunction; these impacts do not register as a concussion on clinical levels.

A review by Bailes et al. (2013) concluded cumulative exposure to the frequent and repetitive head impacts can cause pathophysiological changes to the brain. These pathological changes can be seen in both rodent and human studies. For example a study using rats, by Kanayama et al. (1996) showed, in contrast to single impact, repetitive impacts caused changes in cortical and hippocampal cytoskeletal proteins. After repetitive impacts, rats had impaired ability to habituate to a new environment. Another study, by DeFord et al. (2002), used mice and the Morris water maze and concluded that repeated impacts were associated with decreased spatial learning and cognitive impairment. Although cell death in the cortex, hippocampus or blood brain barrier was not demonstrated. In terms of human research, a study by Talavage et al. (2014) reported neurophysiological changes in high school football players who did not have any observable concussion-like symptoms. Specifically, deficits in visual working memory using the IMPACT test and changes in activation in the dorsolateral prefrontal cortex from pre-season to in-season using fMRI were found. A follow up study by the same authors suggested that it is the

repetitive nature of sub-concussive blows that produce neurological impairment (Breedlove et al., 2012). In this study, pre-season neuropsychological tests and fMRI scans were obtained from all players. Throughout the season, players had head impact monitors on their helmets to record every head contact experience in practice and in games. While in-season, players had additional scans obtained to compare to pre-season scans. There was a significant relationship between the number of blows to the head and neurophysiological changes observed. With an aim of reviewing the available literature, Mainwaring, Ferdinand Pennock, Mylabathula and Alavie (2018) examined sub-concussive head impacts across six sports (football, soccer, hockey, boxing and lacrosse) in a total of 59 studies. Of the 21 neurobiological studies, 17 concluded that prolonged head impacts were associated with structural and some functional changes; imaging modalities included magnetic resonance imaging (MRI), functional MRI and diffusion tensor imaging (DTI). Eight studies examined neurocognitive performance measures, such as verbal learning, memory and processing speed, and a relationship between neuronal damage and performance impairment was found. Interestingly, 14 studies provided support for possible structural changes in players with repeated head trauma without concussion symptoms, including white matter diffusivity, decreased cortical volume, and cortical thinning. Five of the 17 neuropsychological studies found an association between neuropsychological deficits and sub-concussive impacts while three of the 17 had mixed results. Across studies, a variety of established neuropsychological test batteries were used, such as the Automated Neuropsychological Assessment Metric, the Standardized Concussion Assessment Tool (SCAT3) and the Immediate Post-Concussion Assessment and Cognitive Test (ImPACT). The three main cognitive domains assessed were memory, attention and executive function; although there were few significant findings. Even with the significant findings, this evidence is not strongly supported as there was considerable methodological variability and assumptions about head impacts in sports instead of direct measurements. Mainwaring et al. (2018) summarized that in

male athletes, repetitive hits to the head present risk of microstructural and functional changes to the brain, and repetitive head impacts in sports should be avoided.

Mainwaring et al. (2018) have identified 43 different subconcuss* terms in the literature ranging from describing a hit (i.e. sub-concussive hit) to describing damage (i.e. sub-concussive trauma), suggesting a definite definition is still being sought after. Regardless, the role of sub-concussive impacts has been magnified due to the potential of hidden neurological deficits. What is unclear is whether there is a particular concern in soccer, where players are exposed to a high number of head impacts over the course of a season, and thus have the potential to sustain significant sub-concussive damage.

2.2 Heading in Soccer

Soccer is a unique sport given players purposefully and voluntarily use their unprotected heads to manipulate the direction of the soccer ball for both offensive and defensive plays (Kirkendall, Jordan, & Garrett, 2001). On average, players will head the ball six to 10 times per game, with the ball traveling upwards of 80 km (Spiotta, Shin, Bartsch, & Benzel, 2011). Conversely, heading in practice generally consists of repetitive, low velocity heading with a focus on skill development. Acceleration of the head is dependent on the direction of the ball, the spin of the ball and where the ball hits the head on impact. Looking at recorded head acceleration data collected in simulated heading drills with the ball traveling between nine and 12 m/s, linear acceleration of the head has been measured between 15-20 gs ($g = 9.8 \text{ m/s}^2$) and angular acceleration between 1000-2000 rad/s^2 (Naunheim et al., 2003). There is no consensus regarding how much g force causes a concussion; some state the average number of g force for a concussion are between 95g - 100g (Steven P Broglio et al., 2010; Steven P Broglio, Eckner, & Kutcher, 2012; Guskiewicz et al., 2007; Pellman, Viano, Tucker, Casson, & Waeckerle, 2003) while other estimates are lower between 40 – 60 g (McIntosh, McCrory, & Comerford, 2000; Naunheim, R. S., Standeven, J., Richter, C., & Lewis, 2000). Either way, with a maximum of 20 g measured with heading,

this indicates the forces involved in heading in soccer usually falls well below those considered to be required for a concussive impact.

2.2.1 Heading as a Sub-Concussive Impact

There have been several recent systematic reviews that have attempted to determine the effects of soccer heading and sub-concussive impacts; these reviews have yielded mixed results.

Neuropsychological Studies

One of the most recent reviews by Tarnutzer, Straumann, Brugger, & Feddermann-Demont (2017) reported that the frequency of heading was not strongly associated with any neuropsychological impairments. In most of studies, heading was measured using either self-report, observation or a combination of the two; one study used a heading exposure index to determine heading exposure. Of the reviewed studies, 77% (23/30) reported on neurocognitive testing; a combination of case-controlled and cross-sectional studies were examined. A total of 15 studies looked at the possible link between heading exposure and performance on neurocognitive testing; eight studies did not see any differences (Janda et al., 2002; Koerte, Lin, Muehlmann, et al., 2015; Kontos, Dolese, Elbin, Covassin, & Warren, 2011; A Rutherford, Stephens, Potter, & Fernie, 2005; Andrew Rutherford, Stephens, Fernie, & Potter, 2009; Salinas, Webbe, & Devore, 2009; Stephens, Rutherford, Potter, & Fernie, 2010; Straume-Naesheim, Andersen, Dvorak, & Bahr, 2005) while seven studies reported significantly lower results for soccer players than controls in at least one test (Downs & Abwender, 2002; Koerte et al., 2016; Lipton et al., 2013; Matser, Kessels, Lezak, & Troost, 2001; Matser, Kessels, Jordan, Lezak, & Troost, 1998; Witol & Webbe, 2003; Zhang, Red, Lin, Patel, & Sereno, 2013). Of the total number of neurocognitive studies, 78% of studies identified three key cognitive domains commonly affected in sub-concussive impact, including attention, executive function and memory; functions that are mediated by the frontal and temporal lobes. The remaining studies were missing either one or two of the key domains. Results indicated that neurocognitive deficits may be subtle and not identified by all tests. The authors found

various methodological shortcomings. For instance, case-controlled studies that reported neurocognitive deficits had type one errors and inappropriate control groups while empirical studies that demonstrated a correlation between heading frequency and neurocognitive deficits had poor heading assessment criteria. Overall, Tarnutzer et al. (2017) concluded there is weak to no evidence for a link between repetitive impacts in soccer heading and neurocognitive impairments due to methodological issues. Interestingly, 89% of the studies reviewed either did not control for head trauma more than 3-6 months before participation or didn't control for head trauma at all; this results in the inability to distinguish acute repetitive impacts from concussion history.

In a review by Rodrigues et al. (2016), 15 studies investigated the effect of sub-concussive impacts on brain function in both immediate, short-term and long-term exposure; six found significant changes in brain function while nine were non-significant. Of the six studies that found significant changes, there was a mixture of immediate, short-term and long-term. Zhang et al. (2013) investigated the immediate exposure of heading on a novel tablet-based task testing executive function. Matser et al. (1998) investigated the short-term exposure of heading on a battery of neuropsychological tests that looked at memory, planning and visuospatial testing. Three studies investigated the long-term effects of heading on a battery of neuropsychological tests that looked at a combination of attention, concentration, and memory (Tysvaer & Løchen, 1991), motor speed, attention, concentration, reaction time and conceptual thinking (Downs & Abwender, 2002) and attention (Rutherford et al., 2005). The key cognitive domains examined in all studies were attention, memory and concentration. Many of these studies suffered from methodological shortcomings, such as poor control groups and failure to control for history of concussions. Taken together, it appears that neurocognitive deficits may be subtle and hard to detect.

Neuroimaging Studies

In the review by Tarnutzer et al. (2017), there were eight studies that used neuroimaging and six of these studies found significant brain changes in soccer players. Two studies used DTI: Koerte, Ertl-

Wagner, Reiser, Zafonte, & Shenton (2012) found widespread white matter abnormalities although no difference in fractional anisotropy or mean diffusivity, and Lipton et al. (2013) found fractional anisotropy levels were inversely correlated with annual number of headers. Two studies used voxel-based morphology (VBM): Koerte et al., (2016) demonstrated cortical thinning in the right inferolateral parietal, temporal and occipital cortex in soccer players and (Adams, Adler, Jarvis, DelBello, & Strakowski, 2007) showed decreased grey matter density and volume in the anterior temporal cortex. One study used MR spectroscopy (Koerte, Lin, Muehlmann, et al., 2015) and one study used fMRI (Svaldi et al., 2017). Changes were found primarily in the frontal and anterior-temporal regions. Three of the studies using a range of neuroimaging modalities (diffusion tensor imaging, voxel-based morphology and MR spectroscopy) linked structural changes to functional changes, as evidenced by neurocognitive deficits (Koerte et al., 2016; Koerte, Lin, Muehlmann, et al., 2015; Lipton et al., 2013). A correlation between heading exposure and neuroimaging changes were seen in four of the five empirical studies (the same three as above and Svaldi et al., 2017); although the heading exposure assessment was found to be low in quality. Heading was measured with through self-report questionnaires or observation. The methodological issues and small sample sizes limit the support for a link between heading frequency and brain changes.

A review by Rodrigues et al. (2016) suggested the possibility of an association between abnormal brain structure and heading. Four studies used neuroimaging modalities, including head CT (computed tomography), DTI and MRI; three studies analyzed long term exposure study while one looked at short-term exposure. The long-term effect studies had mixed results. Of the two using MRI, one found greater cortical thinning in the right inferolateral-parietal, temporal and occipital cortex of soccer players compared to controls (Koerte et al., 2016) while the other had no difference in brain structure between soccer players and controls (Jordan, Green, Galanty, Mandelbaum, & Jabour, 1996). Koerte et al. (2016) demonstrated cortical thinning was associated with lower cognitive processing speed in the

Trail Making Task and decreased memory performance in the Rey-Osterrieth Complex Figures Test. For short-term effects, Lipton et al. (2013) demonstrated that high frequency of headers (using a questionnaire of 12 months of heading) was associated with impaired white matter integrity (low fractional anisotropy) in the temporo-occipital regions, using DTI, and poor performance in the memory portion of the cognitive battery test CogState.

Limitations in Current Heading Research

Methodological shortcomings seem to be the major issue with sub-concussive impact and soccer heading studies, to date. Research into the effects of repetitive heading is full of mixed results. A multimodal approach to determining the effects of heading is required. Combining neuroimaging and neurocognitive assessment tools while using a suitable control group and controlling number of headers can provide a start to assessing the effects of heading in soccer.

2.3 Purpose of the Current Study

The investigation of the effects of heading in soccer is inconclusive. There needs to be a better understanding of the role of sub-concussive impacts on brain health in a sport that is played by millions of players of all ages every day. Repetitive heading may or may not be a health hazard. The United States Youth Soccer Association seems to lean in favor of a hazard by restricting heading for children ages 11 and 12 while removing heading completely for children ten and under (US Youth Soccer, 2016).

The purpose of this study was to investigate the influence of repetitive heading in youth soccer players using a multimodal approach to examine brain structure and a series of cognitive assessments, including a sideline concussion assessment tool (SCAT-3). The measures used in this study are thoroughly explained next.

Chapter Three: Background

3.1 Evolution of Brain Imaging

Prior to the widespread availability of neuroimaging techniques, researchers relied solely on postmortem investigation to evaluate patients' brains. Neuroimaging has allowed for observation of the brain at the time of injury and while the patient is still alive. Structural brain imaging, like magnetic resonance imaging (MRI), is now a widely available, easily repeatable, non-invasive way to investigate brain pathology. In the 1970s, Paul Lauterbur and Sir Peter Mansfield developed the ability to use MRI to produce images of the body. In 2003, Paul Lauterbur and Sir Peter Mansfield were awarded the Nobel Prize in Physiology or Medicine for their discoveries on magnetic resonance (Nobel Media, 2014). Since then, MRI is used in both research and clinical settings.

3.1.1 Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging (MRI) is a medical imaging technique that uses underlying principles of NMR physics to acquire anatomical images and information regarding physiological processes of the body, in both healthy and diseased state. An MRI scanner uses a strong magnetic field, magnetic field gradients and radio waves to create these images. The main components of an MRI scanner are (McRobbie, 2007):

- 1) main magnet – creates the magnetic field by polarizing the sample; measured in Teslas (T)
- 2) radio frequency (RF) coils – function to both transmit signals and receive signals from the tissue
- 3) gradient system – manipulates the field strength to localize the magnetic resonance signal and the RF signal
- 4) shim coils – adjust the magnetic field to maintain homogeneity
- 5) computers – system controls

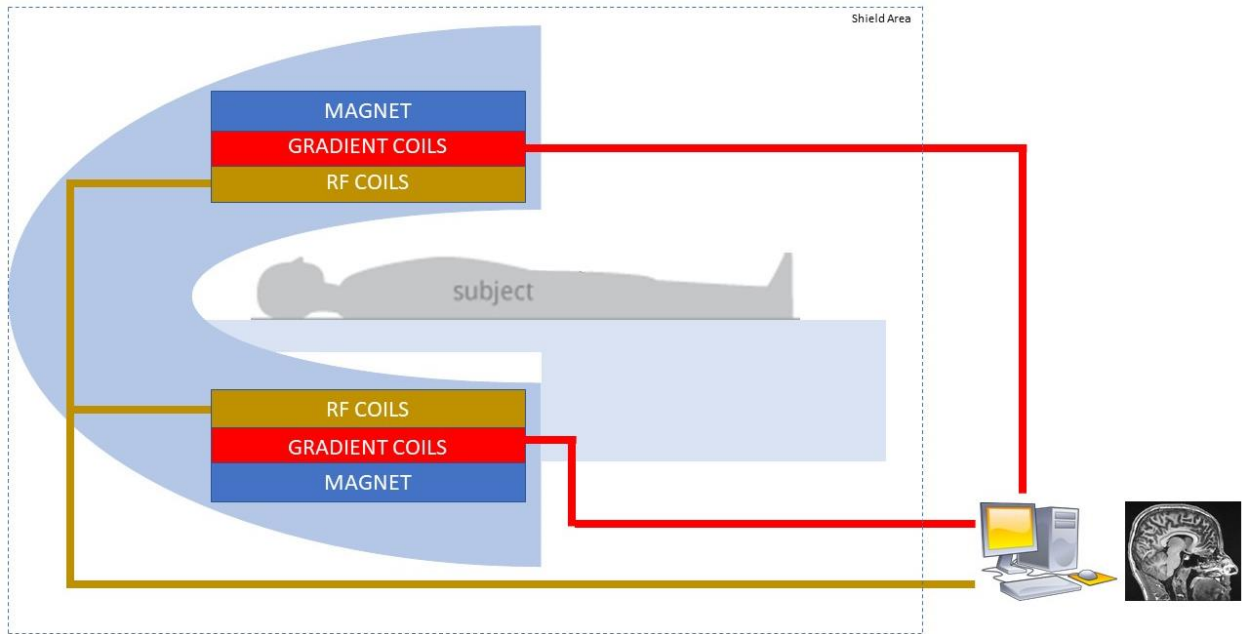


FIGURE 1 COMPONENTS OF A TYPICAL MAGNETIC RESONANCE IMAGING (MRI) MACHINE

Nuclear Magnetic Resonance

MRI uses the principles of nuclear magnetic resonance (NMR; Brown, Cheng, Haacke, Thompson, & Venkatesan, 2014). The human body is comprised almost entirely of water and water is principally made of hydrogen atoms (H_2O).

When exposed to the magnetic field produced by the MRI, the hydrogen ions spin on their axis (called precession) and align either parallel or anti-parallel to the magnetic field. Typically, more nuclei align in their low energy state, parallel (or spin-up) to the main electric field instead of their high energy state, anti-parallel (spin-down) to the magnetic field. When nuclei align parallel, this results in bulk magnetization development.

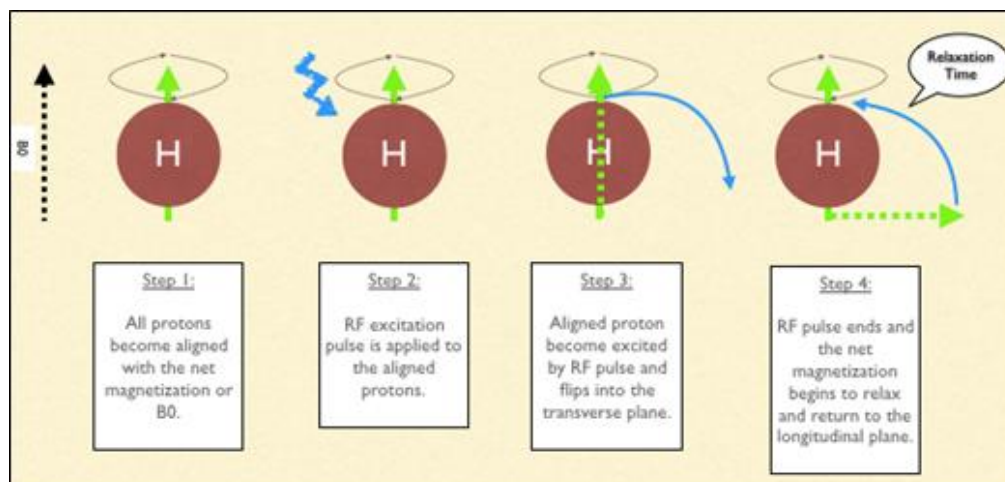


FIGURE 2: DEMONSTRATION OF THE EFFECT OF MAGNETIZATION ON THE SPIN OF A HYDROGEN ATOM (JONES & HUBER, 2018).

The rate of precession is determined by Larmor frequency (ω), which suggests that the rate of the precession is proportional to the strength of the magnetic field (B) and factored by a constant (γ ; the gyromagnetic ratio, equal to 42.57 MHzT^{-1}):

$$\omega = -\gamma B_0$$

In order to measure different brain regions, three linear magnetic field gradients are applied and superimposed in orthogonal directions; the slice selecting gradient, the frequency encoding gradient and the phase encoding gradient. Taken together, these gradients act to create different precession rates at different locations.

T1 Images

Different types of tissue have discrete T_1 relaxation rates depending on the hydrogen density. For example, cerebrospinal fluid (CSF) and blood have a higher hydrogen density than bone. Fluids, like CSF and blood, have long T_1 relaxation rate while fat-based tissues have the shortest T_1 relaxation rate.

In T_1 weighted images, tissues with short T_1 s produce bright contrast while long T_1 produce dark contrast; CSF appears dark grey while white matter and bone appear white (Dale, Brown, & Semelka, 2015). Grey matter appears grey as it has an intermediate T_1 value. T_1 are often known as anatomical scans due to the clear boundaries created by contrast (McRobbie, 2007).

MRI is useful in detecting structural changes to the brain and has been used in studies involving athletes. For example, cortical thinning was found in former soccer players, specifically in the parieto-occipital region, compared to controls (Koerte et al., 2016), using T1 weighted imaging.

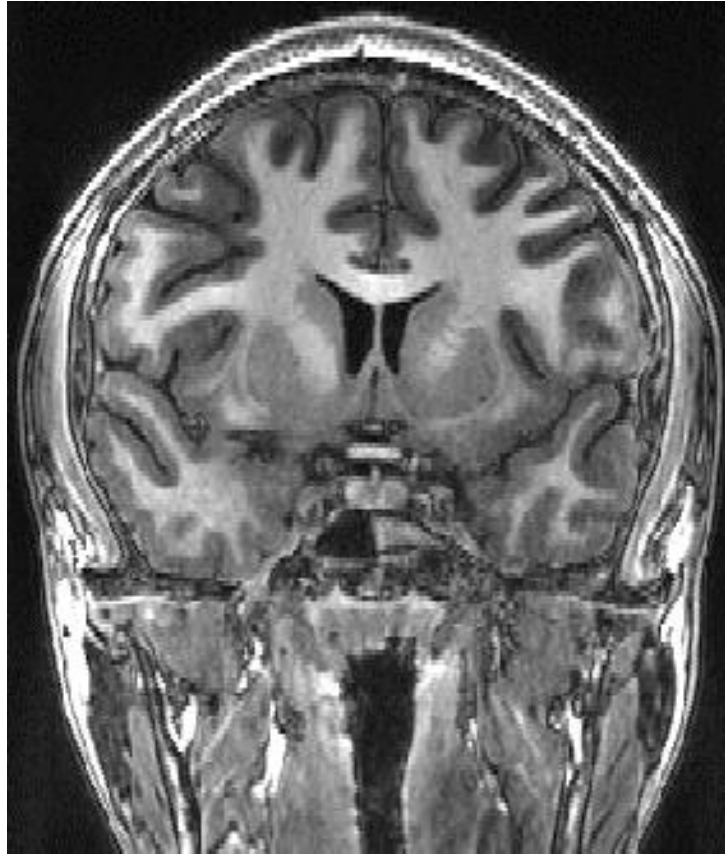


FIGURE 3 AN EXAMPLE OF A SAMPLE T1 MRI SCAN PROVIDING STRUCTURAL INFORMATION. NOTICE THE WHITE MATTER APPEARS WHITE WHILE GREY MATTER IS GREY.

3.1.2 Diffusion Tensor Imaging (DTI)

Recently, there has been a greater focus on a specific variant of MRI called diffusion-weighted magnetic resonance imaging (DW-MRI or DWI), that measures the tissue water diffusion rate. This technique was first used in the 1980s (Bihan & Breton, 1985) and was designed to refine the MRI signal intensity to record the amount of water diffusion. A specific kind of DWI is diffusion tensor imaging (DTI), used to map white matter tractography in the brain (Soares, Marques, Alves, & Sousa, 2013).

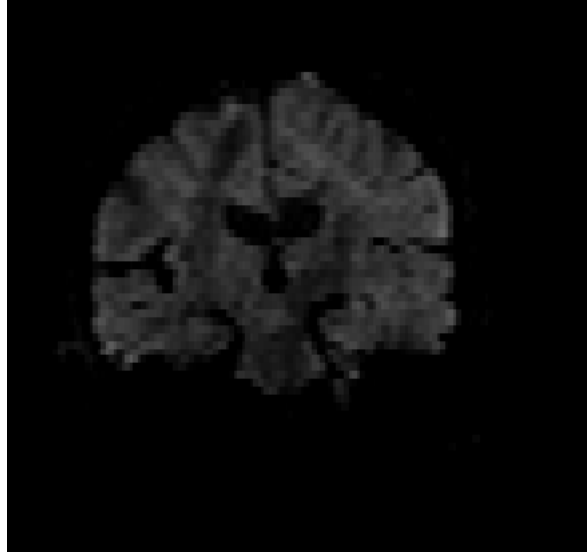


FIGURE 4 AN EXAMPLE OF A SAMPLE DTI SCAN PROVIDING WHITE MATTER TRACT INFORMATION.

Diffusion is the motion of molecules due to kinetic energy via random motion. DTI is specific to the diffusion of water between and within brain cells. The patterns of water diffusion are influenced by tissue type, integrity, architecture and biological barriers (Soares et al., 2013). With no biological barriers to constrain movement, water will diffuse equally in all directions; this is termed isotropic diffusion. Conversely, biological barriers will prevent water from freely diffusing and restrict movement so that diffusion occurs in a parallel direction (e.g. to a fibre bundle); this is termed anisotropic diffusion (Beaulieu, 2002).

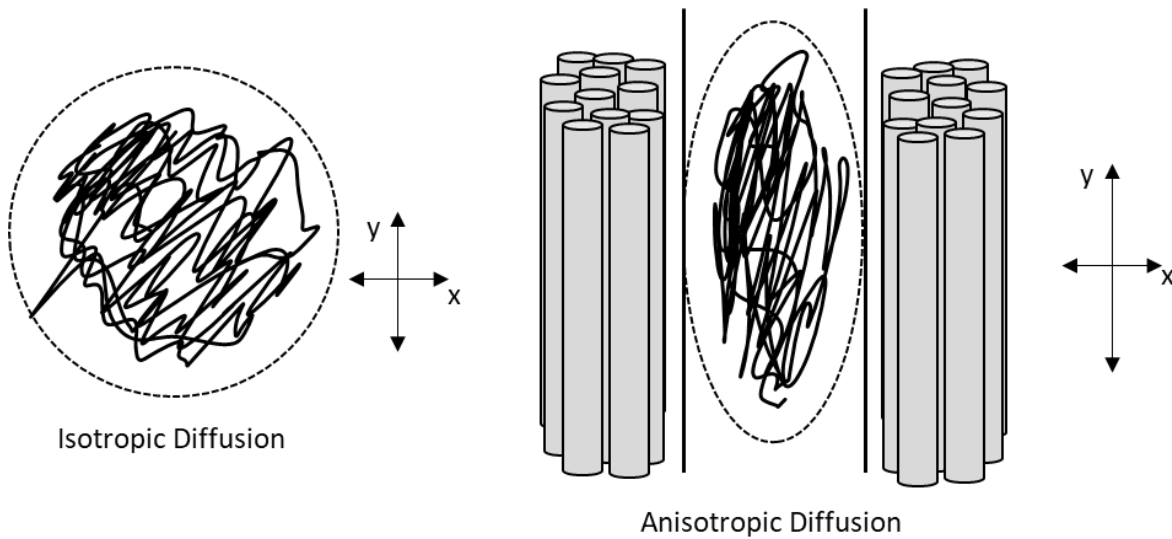


FIGURE 5 AN ILLUSTRATION OF THE FLOW OF WATER WHEN COMPARING FREE MOVEMENT OF WATER (ISOTROPIC) TO RESTRICTED MOVEMENT OF WATER (ANISOTROPIC). THE SPECTRUM OF ANISOTROPY DIFFERENTIATES REGIONS OF WHITE MATTER AND A CHANGE IN ANISOTROPY CAN DEMONSTRATE A CHANGE IN INTEGRITY.

Diffusion Tensor

Diffusion tensor is a mathematical model using a minimum three by three array of numbers that correspond to diffusion rates in a combination of a minimum of six different directions (Alexander, Lee, Lazar, & Field, 2007; P Mukherjee, Berman, Chung, Hess, & Henry, 2008), though 30 directions is more typical. Each element is representative: the diagonal components (D_{xx} , D_{yy} , D_{zz}) represent diffusion coefficients measured along the principal axis (x , y , z), while the off-diagonal components represent the random motion between each pair of principal directions.

$$D = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix}$$

To ensure an ideal frame of reference to view the diffusion tensor, a coordinate system based on the diffusion ellipsoid is used (Jellison et al., 2004; P Mukherjee et al., 2008; Soares et al., 2013). The main principle axis, corresponding to an anatomic feature, is parallel to the principal diffusion direction within each voxel. Three orthogonal unit vectors (ϵ_1 , ϵ_2 , ϵ_3), called eigenvectors, represent the major and minor axes of the diffusion ellipsoid. Each eigenvector has a corresponding value (λ_1 , λ_2 , λ_3), called

an eigenvalue, which define the radius of the ellipsoid (Alexander et al., 2007). Eigenvectors represent the direction of the maximum water diffusion while eigenvalues represent the magnitude of water diffusion (Soares et al., 2013). When comparing isotropic and anisotropic diffusion, the eigenvalues differ (Alexander et al., 2007; Jellison et al., 2004); for isotropic, eigenvalues are close to zero and the diffusion tensor model resembles a circle (see Figure 6), while for anisotropic, eigenvalues are unequal and the tensor model resembles an ellipsoid (see Figure 6). Eigenvalues are influenced by tissue microstructure within the brain and as such, modeling using the diffusion tensor model can be used to detect microstructural changes in the brain in vivo.

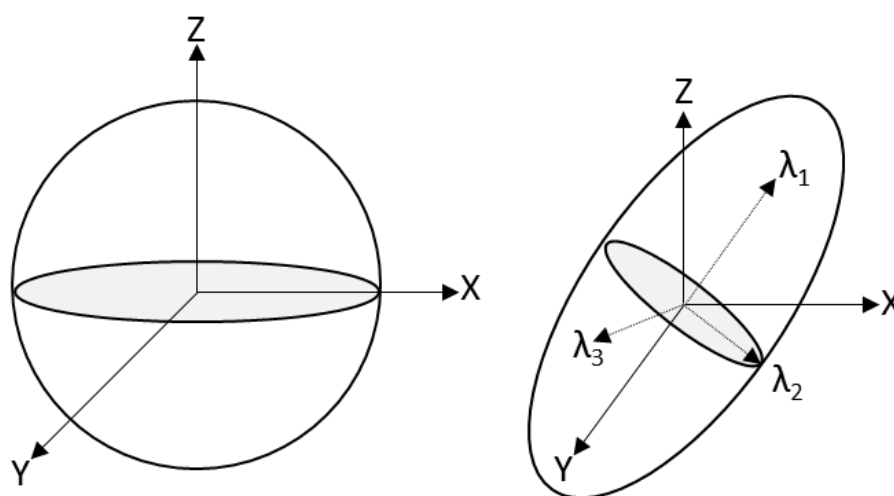


FIGURE 6 GRAPHIC ILLUSTRATION OF THE COORDINATE SYSTEM REPRESENTING THE DIFFERENCE BETWEEN ISOTROPIC AND ANISOTROPIC DIFFUSION

When acquiring DTI data, an initial magnetic field gradient pulse acts on the water molecules, causing the molecules to move out of phase. A second pulse re-phases the water molecules. The displacement of water results in a net phase change, causing an attenuation in MRI signal. Specifically, when the gradients are applied in the same direction as a given bundle of axons, the diffusion that has occurred along the axon bundle results in signal attenuation (in that direction; Alexander et al., 2007; Le Bihan, 2014).

DTI Indices

There are two main diffusion indices based on eigenvalues: mean diffusivity (MD) and fractional anisotropy (FA).

MD is a measure of the water diffusion rate (Soares et al., 2013) and is measure through the following equation, where λ represent the eigenvalues of the diffusion tensor:

$$MD = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3} = \frac{D_{xx} + D_{yy} + D_{zz}}{3}$$

FA is a measure of the amount of diffusion asymmetry, specifically the variation between isotropic and anisotropic diffusion. FA is measured on a scale from zero to one; for perfect isotropic diffusion the value is zero and for anisotropic diffusion the maximum value is one (Mamata et al., 2002; P Mukherjee et al., 2008). FA is calculated with the following formula:

$$FA = \frac{\sqrt{3}}{\sqrt{2}} \sqrt{\frac{(\lambda_1 - MD)^2 + (\lambda_2 - MD)^2 + (\lambda_3 - MD)^2}{(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}}$$

Healthy Human Brain

DTI is used to study healthy brains to compare to pathological populations. In grey matter and CSF, water diffusion is independent of direction and flows freely; diffusion is isotropic and produces a low FA value approaching zero (Assaf & Pasternak, 2008; Jones & Leemans, 2011; Pierpaoli, Jezzard, Basser, Barnett, & Di Chiro, 1996). Conversely, water diffuses parallel to fibre bundles in white matter; diffusion is anisotropic and produces a higher FA value (Jones & Leemans, 2011; Moseley et al., 1990). White matter is highly organized into bundles of axonal fibre tracts and perpendicular water diffusion is restricted by the tightly packed axons and myelin sheaths. In healthy controls aged 20-45, it was reported that the internal capsule had an average FA value of 0.68 +/- 0.07, frontal white matter an average of 0.43 +/- 0.03 and the corpus callosum an average of 0.75 +/- 0.05. (Assaf & Pasternak, 2008; Bammer et al., 2000). Gray matter has low FA due to the presence of cellular structures which obstruct

hydrogen diffusion. MD can be used to analyze structural integrity through water diffusion rates (Jespersen, Kroenke, Østergaard, Ackerman, & Yablonskiy, 2007; Sundgren et al., 2004). Water diffusion in cylindrical structures is slow due to membrane barriers (like myelin-coated axons) that restrict water movement; this is indicated by low MD values and is characteristic of white matter. Conversely, random movement of water molecules in all directions (in other brain structures like extracellular space) results in high MD values; this is characteristic of grey matter.

The reproduced table below provides a simplification of the effects of FA and MD on biological tissues and changes in biological tissues (Alexander et al., 2011).

TABLE 2. FRACTIONAL ANISOTROPY AND MEAN DIFFUSIVITY VALUES OF COMMON CEREBRAL REGIONS AND DISEASE PROCESSES

	FA	MD
Grey Matter	Low	----
White Matter	High	----
CSF	Low	High
High Myelin	High	Low
Dense Axons	High	Low
Axonal Degeneration	Low	High
Demyelination	Low	High

Myelin Damage

Diffuse axonal injury (DAI) has been associated with concussion or mTBI due to the nature of the shearing forces that occur when the head is rapidly accelerated or decelerated (Imajo & Roessman, 1984). DAI produces microscopic lesions and causes myelin loss, axonal degeneration, and axonal swelling; all of these consequences can affect water diffusion (Maruta, Lee, Jacobs, & Ghajar, 2010). Axons are flexible under normal conditions within the brain but become brittle when exposed to the biomechanical forces associated with concussion pathology (D. H. Smith & Meaney, 2000). Within 24 hours after suffering a mTBI, reduced anisotropy in white matter regions has been detected, as compared to controls (Arfanakis et al., 2002), indicating DTI metrics may be sensitive to acute structural

changes. While research into sub-concussive effects and DTI metrics is limited, one study investigated the cumulative heading exposure over a season and noted a decrease in FA when heading exceeded a safe threshold (Lipton et al., 2013).

Myelin is characteristic of white matter and is important when measuring the DTI signal.

Experiments investigating brain development in children showed that anisotropy measures change when myelin is absent (Assaf & Pasternak, 2008; Hüppi et al., 1998; Pratik Mukherjee et al., 2001). Additionally, investigations with MS patients demonstrated anisotropic reduction associated with demyelination (Assaf & Pasternak, 2008; Werring, Clark, Barker, Thompson, & Miller, 1999). A decrease in FA is indicative of loss of biological barriers, like myelin, and represents reduced anisotropic diffusion. As a consequence of a decrease in FA, MD generally will increase; this represents an increase in the rate of water diffusion within the damage tissues (Alexander et al., 2007). Degeneration of fiber bundles may result in a compromise of tissue integrity and thus cause an increase in MD (Vos, Jones, Jeurissen, Viergever, & Leemans, 2012).

A meta-analysis by Aoki, Inokuchi, Gunshin, Yahagi, & Suwa (2012) assessed DTI results in white matter regions of interest (corpus callosum, internal capsule and corona radiata) for those with mild traumatic brain injuries (mTBI). A total of 13 studies were analyzed. Of the 12 studies analyzing on the genu of the corpus callosum, all looked at FA values while four looked at MD values; no significance differences between controls and mTBI patients were observed in the genu of the corpus callosum in 11 of the studies analyzing FA and three of the four studies analyzing MD. All nine studies analyzing the midbody of the corpus callosum looked at FA; minimal reduction in FA values in mTBI patients was found. All studies analyzed the splenium of the corpus callosum and looked at FA while six studies looked at MD values; a significant reduction in FA values were found while in four of the six studies a significant increase in MD values were observed. Six out of the seven studies looking at the internal capsule demonstrated no significant difference in FA values. Three studies looking at the corona radiata

demonstrated no significant difference in FA values. This meta-analysis demonstrates that a lower FA and a higher MD in the posterior corpus callosum may be the most vulnerable to injury and may be the best indicator for an mTBI. DTI is considered a potential biomarker for mTBIs (Bigler & Bazarian, 2010).

Could DTI be a non-invasive one-way to measure acute, sub-concussive heading impacts?

Chapter Four: Methods

4.1 Overview of Experimental Design

The study followed a repeated measure, quasi-experimental design with participants acting as their own controls. The study took place over two consecutive days. On day one baseline data was collected (MRI scan, three behavioural tasks, and the soccer portion including rest, catching, exercise and SCAT-3) and day two post-heading data was collected (soccer portion including rest, heading, exercise and SCAT 3, MRI scan and three behavioural tasks; see Figure 9).

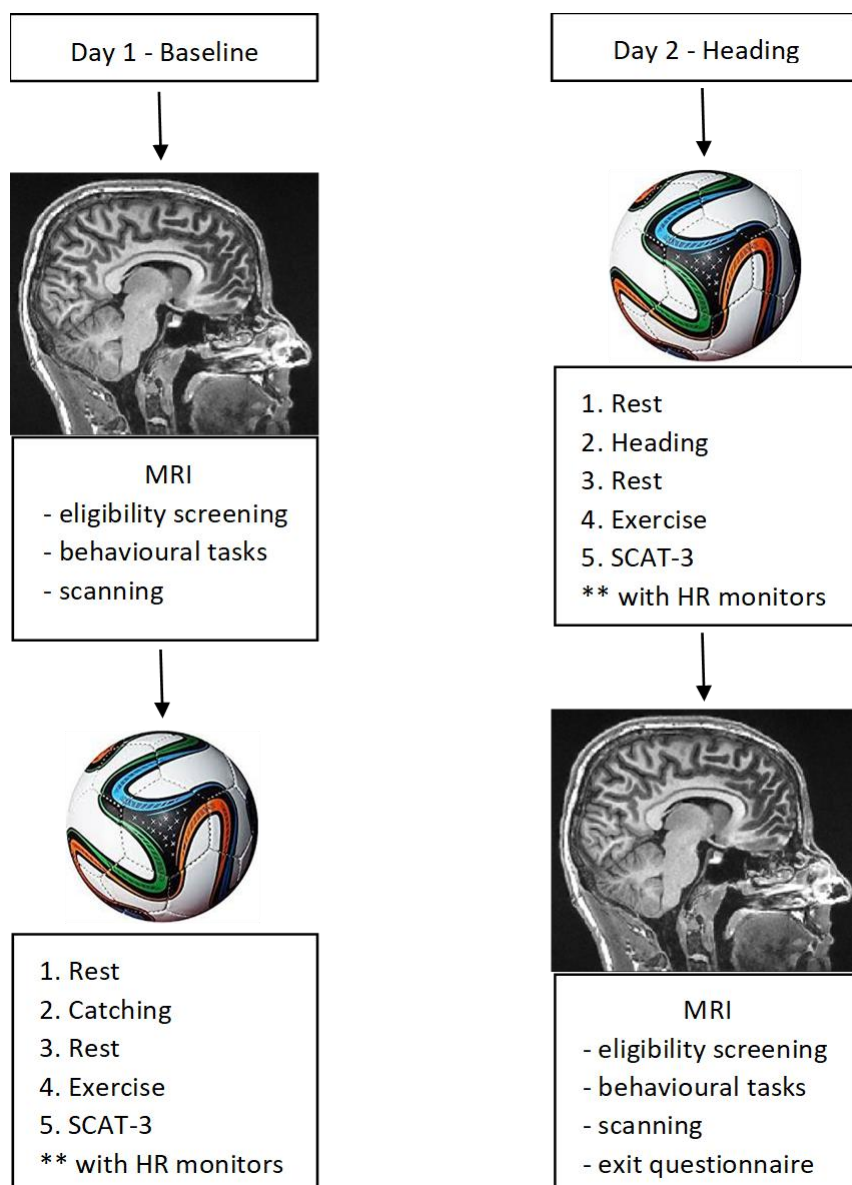


FIGURE 7 ILLUSTRATION OF THE STUDY DESIGN. THE STUDY TOOK PLACE OVER TWO CONSECUTIVE DAYS AND ALL PARTICIPANTS COMPLETED DAY 1 AND DAY 2 IN THE SAME ORDER.

4.2 Study Procedure

The study protocol was approved by the University of Victoria Human Research Ethics Board. Youth participants, aged 15-25, were recruited from Victoria, BC. Testing took place at two primary locations: 1) the MRI scans were done at West Coast Medical Imaging at Uptown Mall in Victoria, BC and 2) Topaz Park in Victoria, BC approximately 5 minutes from Uptown Mall. Participants were included in the study based on the following inclusion criteria: current soccer players (either currently playing or in their

offseason); no current head or neck injury; and no concussion or concussive symptoms within the last six months.

Participants provided informed consent and if under 18, the informed consent was signed by their legal guardian (see Appendix A). MRI screening was administered by an MRI technician before each MRI scan to ensure eligibility (based on having no contraindications for MRI, such as having magnetic metal implants; see Appendix B). Participants also completed a demographic questionnaire (see Appendix C) and medical history form (see Appendix D). To ensure physical readiness (see Appendix D), participants completed a Physical Activity Readiness Questionnaire (PAR-Q+). At the end of the study, participants completed an Exit Questionnaire (see Appendix I). Data were collected over two consecutive days.

4.2.1 Soccer Drills

The drills consisted 5 components: 1) rest 2) catching or heading, 3) rest, 4) steady state exercise and 5) the SCAT-3. These components were completed on both days, with catching on day one for baseline and heading on day two.

- 1) Rest.** During the rest period, participants were instructed to lie completely still for eight minutes. Participants kept their eyes closed and wore ear plugs to minimize environmental noise to ensure complete rest.
- 2) Catching.** A set of cones were spaced 3.65m apart measured with a measuring tape. Participants, in pairs, stood at each end and completed two sets of five catches, switching positions after each set of five. This maintained consistency of direction. The ball was thrown using an underhand toss and participants were instructed to remain standing and catch the ball in front of their heads. Participants mimicked a header before catching the ball right before the ball would hit their head. The ball, a regulation size 5, was inflated to regulation pressure, between 8.5 – 15.6 PSI (International Football Association Board, 2018).

OR

Heading. A similar set-up was used for the heading component on day two. Participants maintained a 3.65m distance and switched positions after every set of five headers. Participants were again instructed to head the ball from standing. Participants wore an accelerometer in a headband to measure the force of the soccer ball. Proper technique was monitored throughout, and improper headers were recorded. If participants missed on a throw or missed on a header, an additional header was added to the rotation. For example, if header number three was missed, then the total number of headers would be 11.

3) Rest. A second eight-minute rest period followed the catching or heading portion of the day.

4) Steady-state exercise. Cones were set up 20 m apart. Participants maintained a constant speed of 20 meters in eight seconds (2.5 m/s) using a High Intensity Interval Training App with an audible reminders (Giorgio Regni, 2015).

5) SCAT-3. At the end of the drills, the SCAT-3 was conducted using standardized instructions for administration and scoring for each section. After administration, the heart rate monitors were removed.

4.3 Acquisition and Analysis

4.3.1 MRI

Acquisition

A 3T GE MRI was used, located at the West Coast Medical Imaging facility located at Uptown Mall in Victoria, BC. Three different types of data were collected: 1) high resolution anatomical image of the brain; 2) diffusion tensor images of the brain; 3) resting state functional magnetic resonance images of the brain. Only the diffusion tensor images was analyzed due to timing. The scanning sessions took approximately ½ an hour to complete. The scan parameters for the 3T GE MRI machine were as followed: acquisition matrix = 256x256, voxel size = 1.4 x 1.4 x 2.0 mm³, TR = 8000 ms, flip angle = 90°,

number of slices = 52. There were 48 images acquired for each scan: 45 diffusion-weighted images ($b = 1000 \text{ s/mm}^2$) and 3 non-diffusion-weighted images ($b = 0 \text{ s/mm}^2$).

Analysis

Image pre-processing. The DTI data was analyzed in Functional MRI of the Brain Software Library (FSL) version 5.0 (Analysis Group, FMRIB, Oxford, UK, <http://fsl.fmrib.ox.ac.uk>; (Smith et al., 2006)). Diffusion weighted images were corrected for head movement and eddy current distortions using Eddy Current Correction, and the skull was removed using Brain Extraction Tool (Smith, 2002). Brain-extracted images were visually inspected to ensure brain tissue was not removed and the images were clear.

Image analysis. DTI fit was used to create FA and MD maps of each individual brain image. Once all FA maps were created, the data was inputted into TBSS to obtain a mean FA skeleton from the projection of all participants' FA data (Smith et al., 2006). Participants' FA data were non-linearly aligned to $1 \times 1 \times 1 \text{ mm}$ standard space; the FMRIB58_FA. Once all individual FA images were aligned to standard space, the mean FA image was created and thinned (threshold FA = 0.2) to generate the mean FA skeleton. A 4D image file was created where each participant's FA data was projected onto the thresholded mean FA skeleton. Voxelwise statistical analysis of the skeletonised FA data was performed using the Randomise function, FSL's nonparametric permutation inference tool. Two design matrix files were created to run a between subjects' analysis. Threshold free cluster enhancement was used to correct for multiple comparisons ($p < 0.05$). In addition to FA data, TBSS was also performed for MD in a similar fashion. Non-linear registration was applied to the MD data and all the participants' MD data was merged into a 4D file. Each participant's MD data was projected onto the mean FA skeleton before applying the same voxelwise statistics.

Statistical comparisons. Within-group comparisons were made between no heading (catching) and heading, on day one and day two respectively. Correlations were made between diffusion metrics of participants (FA; MD) and the SCAT-3 at baseline and day two, separately. The white matter regions

were identified in FSL using the built-in white matter atlas provided by Dr. Susumu Mori at John Hopkin’s University (Hua et al., 2008; Mori et al., 2008; Wakana et al., 2007). Additionally, the corpus callosum was targeted as a region of interest. A brain region mask was created of the entire corpus callosum using FSLmaths and the built-in white mater atlas in FSL. Once the brain mask was created, within-group comparisons were made between no heading (catching) and heading, on day one and day two respectively.

4.3.2 Behavioural Tasks

Three behavioural tasks were used, created using the MATLAB program: 1) the n-back task, 2) the More Than/Less Than task, and 3) the Go/No-Go Task.

Acquisition

N-back Task. Participants were shown a series of letters one at a time at the computer. Participants indicated when the current letter matched the letter shown either 1 or 3 trials before. There were 4 blocks with a total of 150 trials. Between each trial a blank screen was shown (for 1.5 seconds), and total time for the task was approximately 6 minutes.

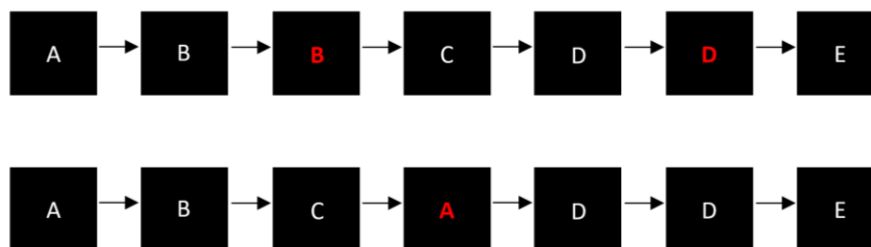


FIGURE 8 THE N-BACK TASK PARADIGM. THE RED COLOUR INDICATES WHEN PARTICIPANTS WOULD HIT THE SPACE BAR TO INDICATED EITHER A 1-BACK RESPONSE (TOP ROW) OR A 3-BACK RESPONSE (BOTTOM ROW)

More Than/Less Than and Odd/Even Task. Both tasks consisted of multiple trials where a single white digit was displayed on a black background. A new digit appeared for each successive trial; the digit disappeared after the participant provided a response. Depending on the task, the words “more less” or “odd even” was displayed below the digit to provide a prompt to the participants regarding task instructions. For the full shifting condition, these two tasks were combined and required participants to

switch from one task to another when a white rectangle surrounds the displayed number. This task consisted of six total blocks; the first two blocks had participants perform the same task (i.e., either all *More/Less* or all *Odd/Even*) while the third to sixth blocks included 10 task-switch trials. Switch trials will occur randomly, with a minimum of 7 to 13 non-switch trials in between each switch. This task took about 6 minutes to complete.



FIGURE 9 THE SWITCH TASK PARADIGM. PARTICIPANTS USED THE A AND L KEY ON A KEYBOARD TO INDICATE RESPONSES. THE SQUARE BOX AROUND THE NUMBER IN THE ODD/EVEN TASK WAS IN PLACE TO ACT AS A SWITCH MARKER.

Go/No-Go Task. The task consisted of two blocks of 50 and 150 trials, respectively; in the first block, participants were asked to respond as quickly as possible to any letter appearing at the centre of the computer screen by pressing the spacebar (i.e., in the “go” condition all trials were “go” trials) to create baseline reaction times. In the second block, participants were asked to do as they did in the first block, except there were instructed to refrain from responding when the letter ‘j’ (the target stimulus) appeared (i.e., the “no go” trials in the “no go” condition). Task completion time was approximately 6 minutes.

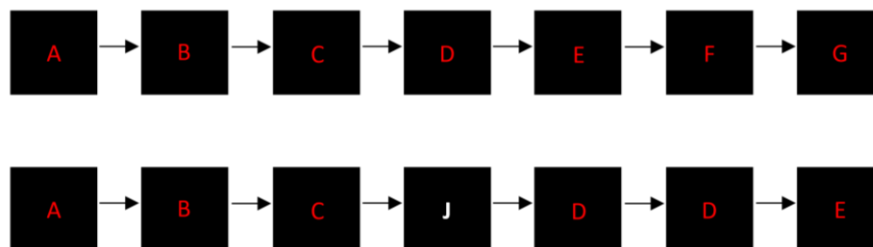


FIGURE 10 THE GO/NO GO TASK PARADIGM. THE RED COLOUR INDICATES WHEN PARTICIPANTS WOULD HIT THE SPACE BAR (ALL THE TIME FOR GO CONDITION ON THE TOP ROW) AND WHITE INDICATES WHEN PARTICIPANTS WOULD REFRAIN FROM HITTING THE SPACE BAR (GO/NO GO CONDITION ON THE BOTTOM ROW)

Analysis

Between-group comparisons were made between day one and day two for all three computer tasks using a between-group paired t-test. The statistical program R was used for analysis (R Core Team, 2013). Each component was compared independently to assess differences between reaction time.

4.3.3 Sports Concussion Assessment Tool 3 (SCAT-3)

Acquisition

SCAT-3 is a standardized sideline concussion assessment tool that was created by the Concussion in Sport Group at the Fourth International Conference on Concussion in Sport (Mccrory et al., 2013). SCAT-3 includes the following evaluations: symptoms, cognitive function, balance control and coordination.

Symptoms and Severity. The symptom rating evaluates 22 different concussion symptoms, each rated on a scale of 0-6. Total number of symptoms and symptom severity are recorded, with higher scores indicating greater number of symptoms and greater symptom severity.

Standardized Assessment of Concussion (SAC). The cognitive assessment consists four different sections that tests orientation, memory, delayed recall and concentration. The SAC is scored out of 30; a higher score indicates better performance. There are three different versions of the memory and concentration tests; alternating lists of words were used for each day.

Balance. The modified Balance Error Scoring System consists of three balance stances (double leg, single leg and tandem stance) held for 20 seconds with eyes closed. The number of errors, indicated as movements from starting position, are recorded. The maximum score for balance is 30, with a higher score indicating more errors.

Coordination. The coordination examination involves five successive finger-to-nose touches, with a maximum score of 5, indicating that the coordination examination was completed correctly

Analysis

SCAT-3 data were compared across the two days using a between-group paired t-test. Each component of the SCAT-3 was compared independently: total number of symptoms and symptom severity were analyzed and compared together, cognitive assessment (SAC) scores were compared, and balance scores were compared.

4.3.4 Polar Heart Rate Monitors

Acquisition

Polar Team Pro heart rate monitors (Polar Team, 2018) were worn throughout the soccer drills, including rest, exercise, catching or heading, and the SCAT-3. Polar Team Pro heart rate monitors were worn to collect heart rate variability (HRV) data in the form of heart rate (beats per minute) and RR intervals (millisecond).

Analysis

Unfortunately, I was unable to analyze the heart rate data as a result of technical difficulties. This data will be analyzed at a later date.

4.3.5 Triax SIM-P Accelerometer

Acquisition

The Triax SIM-P (Triax Technology, 2014) is a highly sensitive impact sensing. The SIM-P was worn using a headband. It recorded all impacts and accelerations greater than a pre-programmed trigger point; for this study, the 10g option was activated.

Analysis

All measurements were transmitted to a Triax app on a iPhone6 in real time and monitored throughout the heading drill. The force heading never exceeded 10g.

Chapter Five: Results

5.1 Participant Characteristics

Eleven participants were recruited for this study; however, one participant was unable to have an MRI scan (due to braces), one participant was unable to complete the exercise portion (due to a lower body injury) and one participant's MRI data was unable to be analyzed. A total of eleven participants were tested, three females and eight males. The participant characteristics are summarized below in Table 2.

TABLE 3 *DEMOGRAPHIC INFORMATION, YEARS PLAYING SOCCER AND CONCUSSION HISTORY OF PARTICIPANTS*

	Group (n = 11)	Females (n = 3)	Males (n = 8)
	Mean (SD)	Mean (SD)	Mean (SD)
Age (years)	20.09 (2.88)	20.33 (4.51)	20 (2.45)
Height (cm)	178.61 (8.45)	172.97 (12.27)	180.72 (6.34)
Weight (kg)	76.45 (12.33)	69.85 (15.60)	78.93 (11.04)
Years Playing (years)	11.36 (4.25)	13.33 (6.66)	10.63 (3.29)
Number of Concussions	1.45 (1.75)	1	1.63 (2.07)

Of the 11 participants, two were left-handed and nine were right-handed. Additionally, the positioning of each participant varied: one played goal, three defense, three midfield, two forward, and two players played multiple positions.

5.2 DTI Data

FA and MD

At the whole brain level, there were no significant differences in FA or MD post heading compared to pre-heading the soccer ball. The FA and MD values of nine participants pre and post heading are summarized in Table 3 below.

TABLE 4 *FRACTIONAL ANISOTROPY (FA) AND MEAN DIFFUSIVITY (MD) VALUE AT THE WHOLE BRAIN LEVEL FOR ALL PARTICIPANTS ELIGIBLE FOR MRI SCREENING. NO SIGNIFICANT DIFFERENCES FOUND BETWEEN GROUPS.*

Participant	Whole Brain FA		Whole Brain MD	
	Pre-heading	Post-heading	Pre-heading	Post-heading
2	0.55480713	0.549174559	0.000712334	0.000715493

3	0.502629434	0.499646352		0.000781202	0.000771834
4	0.526287503	0.529831455		0.000716538	0.000713659
5	0.535925581	0.533491731		0.000728713	0.000718868
6	0.5371087	0.540753377		0.000703857	0.000702866
7	0.515378546	0.51737795		0.000731903	0.000731539
8	0.54868143	0.556450277		0.000683075	0.000692671
9	0.534148043	0.519966366		0.00073616	0.00072788
11	0.5198314	0.532746025		0.000754906	0.000744642

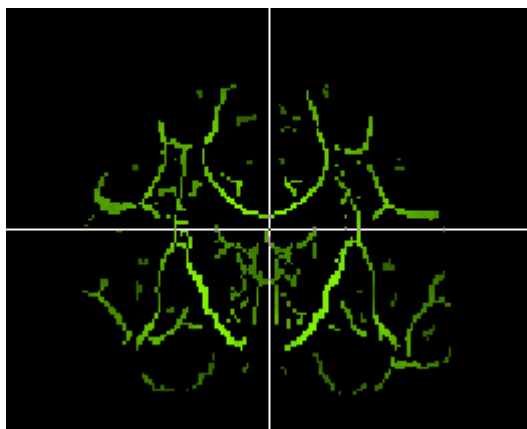


FIGURE 11 REPRESENTATION OF NO DIFFERENCES IN FA DATA FOR ALL PARTICIPANTS BETWEEN PRE AND POST HEADING. THERE IS NO DISRUPTION IN GREEN INDICATING NO CHANGES IN INTEGRITY.

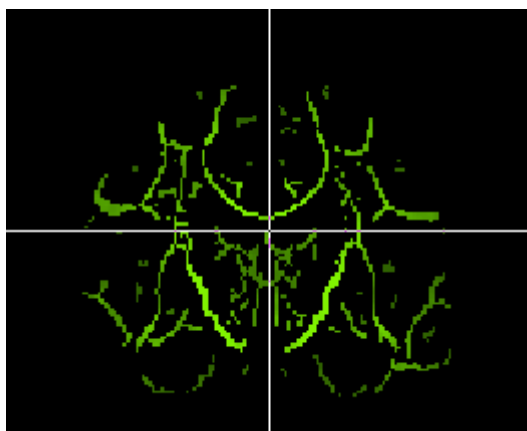


FIGURE 12 REPRESENTATION OF NO DIFFERENCES IN MD DATA FOR ALL PARTICIPANTS BETWEEN PRE AND POST HEADING. THERE IS NO DISRUPTION IN GREEN INDICATING NO CHANGES IN DIFFUSION RATE.

FA, MD and SCAT-3

There were no significant correlations between standardized assessment of concussion scores in the SCAT-3 and whole brain FA or MD either pre or post heading.

Region of Interest: Corpus Callosum

When analyzing the corpus callosum as a region of interest, there were no significant differences in FA or MD post heading compared to pre-heading the soccer ball. The FA and MD values of the nine participants pre and post heading are summarized in Table 4 below.

TABLE 5 FRACTIONAL ANISOTROPY (FA) AND MEAN DIFFUSIVITY (MD) VALUES WITHIN THE *CORPUS CALLOSUM*, A REGION KNOWN TO BE AFFECTED BY A CONCUSSION. NO SIGNIFICANT DIFFERENCE WERE FOUND BETWEEN GROUPS.

Participant	Corpus Callosum FA		Corpus Callosum MD	
	Pre-heading	Post-heading	Pre-heading	Post-heading
2	0.826979419	0.814843153	0.000699079	0.000710056
3	0.785973226	0.775157595	0.000742567	0.000746065
4	0.791553781	0.798667591	0.000727433	0.000726273
5	0.811147696	0.805389537	0.000721623	0.000711717
6	0.799657439	0.80640653	0.000695111	0.000682984
7	0.785738874	0.792348287	0.000713075	0.000711903
8	0.823035476	0.834168126	0.000650102	0.000655533
9	0.79387169	0.772746224	0.000721229	0.000723391
11	0.802432177	0.817042314	0.000732002	0.000709758

5.3 Behavioural Data

N-back Task.

For the N-back 1 portion of the task, there was no significant difference between baseline reaction times ($M=0.4189$, $SD=0.06696$) and post-head impact reaction times ($M=0.4025$, $SD=0.05259$); $t(10)=1.2789$, $p=0.2298$). For the N-back 3 portion of the task, there was no significant difference between baseline reaction times ($M=0.597659$, $SD=0.08242$) and post-head impact reaction times ($M=0.56317$, $SD=0.07413$); $t(10)=1.3633$, $p=0.2027$.

More Than/Less Than and Odd/Even Task.

For the More Than/Less Than portion of the task, there was a significant difference between baseline reaction times ($M=0.546$, $SD=0.0058$) and post-head impact reaction times ($M=0.462$, $SD=0.0439$); $t(10)=4.0275$, $p=0.0024$). Specifically, post-head impact reaction times were less than baseline reaction times. For the Odd/Even portion of the task, there was no significant difference between baseline reaction times ($M=0.628$, $SD=0.139$) and post-head impact reaction times ($M=0.563$,

SD=0.112); $t(10)=1.7457$, $p=0.1115$. For the Switch portion of the task, there was a significant difference between baseline reaction times ($M=0.8427$, $SD=0.185$) and post-head impact reaction times ($M=0.6179$, $SD=0.219$); $t(10)=2.2653$, $p=0.04695$. Specifically, post-head impact reaction times were less than baseline reaction times.

Go/No-Go Task.

Two participants' data were removed from analysis due to faulty data; therefore, only nine participants were included in the behavioural data analysis for the n-back test. For the "Go" portion of the task, there was no significant difference in scores between baseline reaction times ($M=0.1998$, $SD=0.067$) and post-head impact reaction times ($M=0.2037$, $SD=0.0507$); $t(8)=-0.1937$, $p=0.851$. For the "Go-No Go" portion of the task, there was no significant difference in scores between baseline reaction times ($M=0.3495$, $SD=0.0310$) and post-head impact reaction times ($M=0.3559$, $SD=0.0250$); $t(8) = -1.2059$, $p=0.2628$.

5.4 Sport Concussion Assessment Tool – 3rd Edition Data

Symptoms and Severity. No significant differences between baseline reaction symptom scores ($M=2.55$, $SD=4.03$) and post-head impact symptom scores ($M=1$, $SD=1.67$); $t(10)=1.648$, $p=0.130$). No significant differences between baseline reaction severity scores ($M=2.73$, $SD=4.15$) and post-head impact severity scores ($M=1.18$, $SD=1.78$); $t(10)=1.584$, $p=0.144$). Finally, when symptoms and severity were combined into one score, there was no significant differences between baseline reaction symptom and severity scores ($M=3.27$, $SD=3.38$) and post-head impact symptom and severity scores ($M=2.18$, $SD=1.99$); $t(10)=1.707$, $p=0.119$).

Standardized Assessment of Concussion (SAC) . A significant difference between baseline SAC cognitive function scores ($M=27.18$, $SD=1.47$) and post-head impact SAC cognitive function ($M=28.55$, $SD=1.04$); $t(10)=-4.404$, $p=0.001$). Specifically, post-head impact SAC cognitive function scores were greater than baseline scores.

Balance. No significant differences between baseline balance scores (M=3.27, SD=3.37) and post-head impact balance scores (M=2.18, SD=1.99); $t(10)=1.71$, $p=0.1186$).

Coordination. All participants scored the same on baseline and post-head impact coordination scores.

TABLE 6 SCAT3 AVERAGE SCORES ACROSS ALL ELIGIBLE PARTICIPANTS

Day 1		Day 2	
Symptoms	2.545	Symptoms	1
Severity	2.727	Severity	1.3
Standard Assessment of Concussion	27.182	Standard Assessment of Concussion	28.545
Orientation	5	Orientation	5
Immediate Memory	14.545	Immediate Memory	14.909
Concentration	3.545	Concentration	4.455
Delayed Memory	4.091	Delayed Memory	4.182
Balance Errors	3.273	Balance Errors	2.182
Coordination	1	Coordination	1

5.5 Triax Sim-P Accelerometer

The accelerometer was set to record any impacts greater than 10g. The heading portion of the soccer drills never exceeded the minimum threshold of 10g, thus no impacts were recorded for any participants in this study.

Chapter Six: Discussion

The purpose of this study was to investigate the effects of heading in youth soccer players with a multimodal approach, examining brain structure, heart rate variability and a series of cognitive assessments, including a sideline concussion assessment tool (SCAT-3). Due to equipment failure, heart rate variability was not analyzed; although, the data was collected and is stored. Therefore, three out of the four research questions were addressed: 1) does heading cause a significant change in brain structure post-heading as analyzed through DTI analysis; 2) does heading cause a change in cognition as assessed using three behavioural computer tasks; and 3) does heading cause differences in performance as measured by the SCAT-3. At the whole brain level, no significant differences in brain structure were observed between baseline and post-heading. Significant differences were observed in one of the three behavioural tasks (the Odd/Even task); improvement was seen post-heading, indicating heading did not result in a negative change in cognition. Similarly, a significant difference was observed in one of the four sections of the SCAT-3 (the SAC); improvement was seen post-heading, indicating heading did not result in a negative change. There were no significant differences between baseline and post-heading in the other two behavioural tasks and the rest of the SCAT-3.

6.1 Brain Structure and Heading

No significant differences were found in FA or MD post-heading compared to baseline at the whole brain level. Additionally, there were no significant correlations between brain structure (as measured by DTI) and SAC cognitive function scores in the SCAT-3 and FA or MD for either baseline or post-heading. The results suggest that repetitive heading in soccer practice, under 10g, does not contribute to structural changes at a whole brain level.

There is limited research investigating heading as a controlled intervention in soccer players using DTI to measure brain structure before and after heading. Previous research has used self-report questionnaires

and observation by coaches and/or research to measure the amount of heading by participants. Self-report and observation do not provide the ability to control the number of headers a participant experience. To date, this is the first study to control the number of headers and mimic a soccer practice setting. The only other known DTI study with heading in soccer is a study by Lipton et al. (2013) which found heading to be associated with lower FA in three locations in the temporal-occipital white matter. Heading was quantified using self-report heading over the previous twelve months, with an average of 442 headers. Interestingly, the reported brain abnormalities were seen opposite of heading impact suggesting a countercoup injury (coup injury occurs at site of impact while countercoup is opposite to impacts). Lipton et al. (2013) performed a longitudinal study over a year using self-reported heading in both practice and game. The current study only looked at 10 headers in a practice setting. The game setting may contribute to the countercoup injury due to increased ball velocity and g force to the head.

6.2 Brain Function and Heading

In this study, three behavioural tasks were used to evaluate brain function: 1) the N-back test, 2) the Go/No Go task and 3) a Switch task using More Than/Less Than and Even/Odd subtasks. Of the three main tasks, no significant differences were found between baseline and post-heading scores. Significant differences were found between baseline and post-heading in the More Than/Less Than subtask of the Switch task. Specifically, participants did better post-heading, indicating there is a potential practice effect. The results of the current study indicate no acute cognitive changes occur post-heading in a soccer practice setting. Previous research has indicated that neurocognitive testing may be subtle and hard to detect.

The behavioural tasks in the current study do align with key cognitive domains highlighted in recent literature reviews on repetitive heading (Rodrigues et al., 2016; Tarnutzer et al., 2017). The N-back is a measure of working memory and is designed to determine how well participants are at updating,

holding, and discarding information. The N-back has been reported to be sensitive to the effects of neurotrauma (Chen, Johnston, Petrides, & Ptito, 2008) and repetitive sub-concussive blows (Talavage et al., 2014b). This study does not demonstrate impairment in working memory as measured by the N-back task. The Go/No Go task is designed to measure response inhibition and impulse control. Response inhibition can be momentarily impaired following a concussion (Covassin, Moran, & Wilhelm, 2013; Karr, Garcia-Barrera, & Areshenkoff, 2014) although there is no research to-date exploring response inhibition in sub-concussive effects. The current results do not demonstrate impairment in response inhibition as measured by the Go/No-Go task. The Switch task, including the More Than/Less Than and Odd/Even subtasks, is used to examine task shifting ability. In order to switch between tasks, participants need to reallocate their attention, inhibit rules learned from the previous task and retrieve rules for the current task while constantly monitoring and detecting conflicts (Friedman et al., 2008). Some studies have found a significant effect of repetitive heading on attention (Rutherford et al., 2005; Stephens, Rutherford, Potter, & Fernie, 2005).

The results in the current study do not show post-heading detriments. The literature investigating the effects of heading on cognitive function is mixed, as mentioned earlier. Some studies have demonstrated potential negative effects of heading on memory and concentration (Downs & Abwender, 2002; Matser et al., 2001, 1998; Webbe & Ochs, 2003) while other studies have found no effects from heading on the same domains (Guskiewicz et al., 2007; Kaminski, Wikstrom, Gutierrez, & Glutting, 2007). The Immediate Post-Concussion Assessment and Cognition Testing (ImPACT) is a popular concussion assessment tool and measures verbal memory, visual memory visual-motor speed, reaction time and impulse control. Studies utilizing the ImPACT measurement found no significant difference between baseline and heading (Gutierrez, Conte, & Lightbourne, 2014; Kontos, Dolese, Elbin Iii, Covassin, & Warren, 2011; Zuckerman et al., 2012). The mixed results seem to stem from the variability

of neuropsychological testing used in each study. In order to compare results and come to conclusions, common methodology needs to be employed.

6.3 SCAT-3 Performance and Heading

Significant difference from baseline to post-heading were found for the Sideline Assessment of Concussion (SAC) portion of the SCAT-3. Specifically, cognitive assessment scores after heading were better than baseline catching scores; this result suggests a possible practice effects. In a study by McCrea (2001) looking at mental status testing after sport-related concussion, it was found that uninjured controls demonstrated a statistically significant improvement in SAC scores from baseline to 48hours later. Conversely, Valovich, Perrin, & Gansneder (2003) found no practice effects with repeated administration on uninjured athletes. The SAC portion of the SCAT-3 tests memory (both short and delayed), orientation and concentration. The memory and concentration components have three alternate forms of the test, which is designed to minimize practice effects. With the alternate forms of the test, the practice effects may be due to strategies employed by participants. Our results indicate participants did better in memory and concertation on day two, with concentration showing the greatest mean improvement (see Table 1). While the results in the current study show improvement on day two, this still provides support that heading is not a cause for a decline in cognitive performance. Similar to the current study, a study by Dorminy et al. (2015) found no significant effects of heading on cognitive performance when using the SCAT-2, a previous version of the SCAT (McCroory et al., 2009). While this study used the SCAT2, the SCAT3 does not differ in the symptom, cognitive or balance components and thus these results are comparable to the current study. Zimmer, Marcinak, Hibyan, & Webbe (2015) collected SCAT2 data on 447 college athletes (mean age 19.24) and calculated an average SAC score of 27.17 (SD=4.07); our results fall near this average showing the participants in this study do not differ from an average uninjured sample.

The other components of the SCAT3 (including symptoms, symptom severity, balance and coordination) did not result in significant differences from baseline to post-heading testing days. The effect of heading on concussion-like symptoms mixed. Some studies identify an increase in symptoms after bouts of heading (Dorminy et al., 2015; Janda et al., 2002; Schmitt, Hertel, Evans, Olmsted, & Putukian, 2004) while others indicate no changes pre and post-heading (Kontos, Dolese, Elbin, et al., 2011; Putukian, Echemendia, & Mackin, 2000) A systematic review by (Kontos et al., 2017) states there is no conclusive finding for the effect of heading on concussion-like symptoms. A normative sample of uninjured college-aged athletes found the average amount of symptoms to be 1.75 (SD=3). In this study, there was no significant difference in symptom reporting or severity of symptoms reported. The symptom and severity reporting in this study were higher at baseline than post-heading, indicating heading did not cause concussion-like symptoms. The literature on the effects of heading on balance is mixed as well. Some research indicates there is impairment in balance post-heading (Haran, Tierney, Wright, Keshner, & Silter, 2013; Hwang, Ma, Kawata, Tierney, & Jeka, 2017; Kaminski, Cousino, & Glutting, 2008) while others have found no impairments (S P Broglio, Guskiewicz, Sell, & Lephart, 2004; Dorminy et al., 2015; Mangus, Wallmann, & Ledford, 2004). Valovich, Perrin, & Gansneder (2003) found a slight practice effect in repeated administration of the balance portion in the SCAT in uninjured high school athletes over a 7-day period. In this study, there was no significant difference between baseline and post-heading in balance.

6.4 Strengths

This study used a multimodal approach, encompassing both brain structure and function, to analyze the effects of repetitive heading. The protocol was optimized to limit potential confounding variables. Participants acted as their own controls. Baseline and post-heading MRI scans were obtained within 24 hours of each other and MRI scan post-heading were obtained within four hours of heading the ball. The heading protocol used in this study mimicked a heading drill used by soccer teams in practice.

6.5 Limitations

The sample size of the current study was small, although imaging studies generally have smaller numbers (Hayasaka, Peiffer, Hugenschmidt, & Laurienti, 2007). The small sample size does affect the power to detect effects in the behavioural tasks and the SCAT-3 analysis, therefore the results must be interpreted with caution. The sample chosen for the study was a convenience sample as all participants were youth soccer players in Victoria. This study focused on a practice setting and results cannot be applied to a game day environment. Games have fewer number of headers with greater velocities and head acceleration. Additionally, the protocol only had ten headers. The number of headers may differ per team and per practice. The condensed protocol schedule was designed to minimize confounding variables, but the study did not directly control for participating in other activities. Participants could have been exposed to additional head-impacts in their daily sport participation. Additionally, it is possible that the participants had microstructural damage from previous soccer play and there was no noticeable difference due to one practice setting.

One of the original purposes of the current study. There was an inability to analyze the heart rate variability collected on both days. Due to equipment malfunction, the HRV data was unable to be retrieved from the heart rate monitors. The heart rate monitors were sent to Polar for troubleshooting and this data will be analyzed later. Therefore, heart rate variability was unable to be compared to DTI data and cognitive data.

6.6 Future Research

This study was just the beginning in determining the effects of heading in soccer on brain structure and cognitive function. Future research should investigate these effects in a full practice setting as well as in game setting as the number of headers, velocity of the soccer ball, and head acceleration differ between isolated drills, full practice and games. Additionally, comparing soccer players to other sports

will be crucial in teasing about the role of soccer heading as a sub-concussive effect compared to other repetitive head impacts, such as those found in football and hockey.

DTI data is emerging as a biomarker for concussion and sub-concussive research. Future studies can explore regions are interest, such as the corpus callosum and other white matter tracts. Additionally, functional MRI data can be explored to determine the changes in functional brain networks after a bout of heading.

The current study had a small sample size. Future research should add more participants to increase power and generalization. Due to the small sample size, there was not enough participants to analyze sex differences. A study by Bretzin, Mansell, Tierney, & McDevitt (2017) determined that neck girth and neck strength may effects the kinematics of heading, such that stronger muscles may lower linear acceleration. Bretzin et al. (2017) found a significant difference between sexes in both neck strength and neck girth.

Additionally, a longitudinal study evaluating the effect of repetitive heading over the course of multiple seasons and years of playing will be important to establish the long-term effect of heading in soccer.

Chapter Seven: Conclusions

Due to the inconclusive nature of previous research into effects of heading in soccer, the current study attempted to provide new direction in sub-concussive research. The purpose of this study was to investigate the influence of repetitive heading in youth soccer players using a multimodal approach to examine brain structure, heart rate variability and a series of cognitive assessments, including a sideline concussion assessment tool (SCAT-3). Unfortunately, due to equipment malfunction, heart rate variability data was not part of the final assessment, although the data will be analyzed in the future. Repetitive heading may or may not be a health hazard. The United States Youth Soccer Association has restricted heading for children ages 11 and 12 while removing heading completely for children ten and under (US Youth Soccer, 2016). This study imitated a practice setting in youth soccer and found no evidence in brain structure or cognitive function after a round of heading compared to baseline. Heading in practice does not seem to cause changes in brain structure and cognitive function. Future research should investigate heading in games with a focus on a multimodal approach, increased sample size and investigate both acute and longitudinal effects.

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Appendix A: Ethics Approval



Office of Research Services | Human Research Ethics Board
 Michael Williams Building Rm B202 PO Box 1700 STN CSC Victoria BC V8W 2Y2 Canada
 T 250-472-4545 | F 250-721-8960 | ethics@uvic.ca | uvic.ca/research |

Certificate of Renewed Approval

PRINCIPAL INVESTIGATOR: Brian Christie UVic STATUS: Faculty UVic DEPARTMENT: MEDS	<table border="1"> <tr> <td>ETHICS PROTOCOL NUMBER:</td> <td>16-170</td> </tr> <tr> <td colspan="2">Above Minimal Risk Review</td> </tr> <tr> <td>ORIGINAL APPROVAL DATE:</td> <td>17-Jun-16</td> </tr> <tr> <td>RENEWED ON:</td> <td>09-Jun-17</td> </tr> <tr> <td>APPROVAL EXPIRY DATE:</td> <td>16-Jun-18</td> </tr> </table>	ETHICS PROTOCOL NUMBER:	16-170	Above Minimal Risk Review		ORIGINAL APPROVAL DATE:	17-Jun-16	RENEWED ON:	09-Jun-17	APPROVAL EXPIRY DATE:	16-Jun-18
ETHICS PROTOCOL NUMBER:	16-170										
Above Minimal Risk Review											
ORIGINAL APPROVAL DATE:	17-Jun-16										
RENEWED ON:	09-Jun-17										
APPROVAL EXPIRY DATE:	16-Jun-18										
<p>PROJECT TITLE: The Effects of Multiple Sub-Concussive Impacts during Heading in Soccer on Heart Rate Variability and Cognition</p> <p>RESEARCH TEAM MEMBER Co-principal Investigator: Rebecca Kenny (Graduate Student, UVic); Samantha Kennedy (Student, UVic); Caroline Spaner (Student, UVic); Dr. Brian Christie (Investigator, UVic); Dr. Lynne Stuart-Hill, Collaborator (UVic)</p> <p>DECLARED PROJECT FUNDING: None</p>											
<h4>CONDITIONS OF APPROVAL</h4>											
<p>This Certificate of Approval is valid for the above term provided there is no change in the protocol.</p> <p>Modifications To make any changes to the approved research procedures in your study, please submit a "Request for Modification" form. You must receive ethics approval before proceeding with your modified protocol.</p> <p>Renewals Your ethics approval must be current for the period during which you are recruiting participants or collecting data. To renew your protocol, please submit a "Request for Renewal" form before the expiry date on your certificate. You will be sent an emailed reminder prompting you to renew your protocol about six weeks before your expiry date.</p> <p>Project Closures When you have completed all data collection activities and will have no further contact with participants, please notify the Human Research Ethics Board by submitting a "Notice of Project Completion" form.</p>											
<h3>Certification</h3>											
<p>This certifies that the UVic Human Research Ethics Board has examined this research protocol and concluded that, in all respects, the proposed research meets the appropriate standards of ethics as outlined by the University of Victoria Research Regulations Involving Human Participants.</p> <p style="text-align: center;">_____ Dr. Rachael Scarth Associate Vice-President Research Operations</p>											

Certificate Issued On: 09-Jun-17

16-170 Christie, Brian



University
of Victoria

Appendix B: Informed Consent

Consent Form

The Effect of Multiple Sub-Concussive Impacts during Heading in Soccer on Brain Structure and Function

Why Are You Being Given This Document

You are being invited to participate in a **research study**. Please take your time to review this Research Study Summary and Consent Form and discuss any questions you may have with the research team. You may wish to discuss it with your friends, and family before you make your decision. Please ask the research team to explain any words or information that you do not clearly understand. Your participation in this study should be purely voluntary.

Research Team:

Name	Organization	Role	Contact Information
Dr. Jodie Gawryluk	University of Victoria	Principal Investigator	
Dr. Mauricio Garcia-Barrera	University of Victoria	Co-Investigator	
Chantel Mayo, M.Sc.	University of Victoria	Graduate Student	
Lisa Ohlhauser, B.Sc.	University of Victoria	Graduate Student	
Rebecca Kenny, B.Sc	University of Victoria	Graduate Student	
Victor Skrzypczynski	University of Victoria	Research Assistant	

You may contact the research team if you have any questions by either email or phone using the above contact information.

This research is being funded by the University of Victoria.

What Is The Research About?

Sub-concussive impacts can occur when an individual's head makes contact with a ball, which commonly occurs in contact sports. However, little is known about the effects of sub-

concussive impacts on brain structure and function (e.g. does heading the ball change the way that the brain looks or the way that the brain works?). The most recent research in this area has used functional neuroimaging techniques (i.e. brain scans) to detect changes in brain activity after playing sports. The objective of the current study is to use structural and functional neuroimaging to examine changes in brain structure and activity before and after soccer practice that includes heading the ball. This study will also compare 15 youth soccer athletes before and after heading practice. Magnetic resonance imaging (MRI) scans allow for the visualization of the brain and will be used to examine brain activity (using a technique called functional MRI) and the connections between different brain regions (using a technique called diffusion tensor imaging). Both of these techniques are types of MRI scans that require you to lay still while pictures are taken of your brain. In addition to collecting brain images, we also ask that you complete several pencil and paper questionnaires and three short (20 minutes in total) computer tasks that will help us understand the brain scans. The results of this study could help us better understand the effects of sub-concussive impact on the brain.

You should be aware that your results are confidential (this information will not be shared with anyone, with an exception for incidental findings).

You should also be aware that this is a research study and that the images that will be taken **have not been approved for medical diagnosis.**

Am I Eligible to Participate?

You are being asked to participate in this study because we are tracking changes in your brain before and after soccer heading practice.

- You **may** participate if you are at least 15 years of age and able to complete study related tasks without assistance.
- You **may not** participate if you have one of the conditions listed in Table 1. A member of our research team as well as an MRI technician will confirm that you do not have any of these conditions before you can participate.

TABLE 1

You may not participate in this study if you have metal objects inside your body. MRI can be dangerous for anyone with metal implants or metal objects inside their body. The following list is not necessarily complete. Please discuss with your physician and/or the research team if you have or may have any object in your body that was not there when you were born.

- Surgery involving metal, such as: clips, rods, screws, pins, wires.
- Heart pacemaker
- Implanted electrodes, pumps or electrical devices
- Cochlear (inner ear) implants
- Intraocular lens (eye) implants (Cataract lenses are allowed if they are soft lenses)
- Any metallic foreign body, shrapnel or bullet (Please mention if you have ever been a grinder, metal worker, welder, wounded during military service, etc.)
- Intrauterine contraceptive device (IUD) or contraceptive diaphragm

- Dental work held in place by magnets
- Non-removable dental braces and retainers
- Metal dental work, unless it is composed predominantly of precious or semiprecious alloy or amalgam (including multiple crowns or bridges)
- Tattooed eyeliner
- Some tattoos (depending on the location and color of the ink - if you do have a tattoo, please discuss with the research team)
- Non-removable metal jewelry (body piercing)
- Nicotine and/or contraceptive patches

You may not participate in this study if, in the opinion of the screener, you have a medical condition that could be made worse by any stress associated with participation in a research protocol. These conditions include:

- heart and circulatory problems
- seizure disorders
- anxiety disorders
- mental disorders

You may not participate in this study if have claustrophobia.

What Will I Be Asked to Do?

If you agree to voluntarily participate in this research, your participation will include the following:

- You will be asked to complete two MRI scanning appointments (1 hour each; details below) and one heading practice (30 minutes)

MRI Scanning Appointment(s)

- You will be asked to review a preliminary screening form for your safety. You will be asked various questions and complete another more detailed screening form before your appointment to make sure that there are no metal objects in your body, so that it is safe for you to have an MRI scan done.
- At your appointment for the MRI scan, you will be asked screening questions again. Be aware that you will be asked the same questions more than once. Since safety is a concern for all participants, we want to make sure that we are covering all the bases of MRI screening.
- You will also be asked to complete a questionnaire regarding your history of concussion.
- Before the MRI scan, you will be asked to complete three computer tasks that will take approximately 6 minutes each. The tasks will involve viewing a computer screen and responding to pictures that you see by pressing buttons on a keyboard. One task will ask you to indicate when the current letter matches the letter shown either 1 or 3 trials prior. Another task will ask you to decide whether a number is more or less than another number or if it is odd or even. A final task will ask you to press a button for every letter except for a target letter. These tasks will be described to you in more detail

before you participate in the study. You will also have a chance to practice these tasks and ask any questions that you may have before you take part in the study.

- After the computer tasks, the research team and trained MRI technician will show you the MRI system.
- You will be asked to wear clothing that does not contain metal. You can wear your own clothing, if it is metal-free (e.g., jogging suit) or the hospital gowns that we can provide. Before you enter the MRI room, we will ask you to remove all metal objects, (hearing aids, dentures, partial plates, keys, cell phone, eyeglasses, hair pins, barrettes, jewelry, body piercing jewelry, watch, safety pins, paperclips, money clip, credit cards, bank cards, magnetic strip cards, coins, pens, tools, clothing with metal fasteners & clothing with metallic threads) since these objects could be attracted to the MRI scanner with great force and cause serious injury if a metal object hit anyone in the way. You will be given a secure place to store your personal items.
- You will be positioned comfortably on your back on a bed, which will be slid into the large, tunnel-shaped scanner until your head is at the centre of the magnet.
- Various types of banging noises are produced by the MRI machine. You must wear carefully fitted ear plugs and head phones (supplied by the researchers) during the MRI to reduce the noise from the scanner and protect your hearing from any damage. The headphones also allow us to communicate with you. You will also wear a microphone that enables you to talk to the researchers while your head is in the scanner.
- During the scan, the MRI technician will talk with you regularly through the two-way intercom to let you know what to do and to check on your comfort. You will also have a squeeze-bulb alarm that you can use at any time to signal the researchers that you want the session to end.
- At times you will be asked to remain very still so that the images will be sharp.
- After the second scan has been completed and you have left the MRI room, we will ask you to fill out a questionnaire about how the study session went for you.



3 Tesla MRI system

The tunnel is 60 cm (about 2 feet) across and is open at both ends.

Heading Practice

- You will be asked to participate in a heading practice (30 minutes) located where you typically have your soccer practices, if possible. This heading practice will occur in between

your two MRI scans. To measure the force of the ball, you will be wearing a headband accelerometer.

- You will begin with 5 minutes of rest.
- Next, you and another participant will take turns tossing and heading the ball to one another; you will toss the ball to them, and they will head the ball back to you, and then you will switch. In total, you will head the ball back to your partner approximately 10 times.
- You will then rest for 5 minutes
- We will complete the practice with a brief pen and paper – based test called the SCAT-3.
- Please note that the current study is not proposing that you incur “additional heading” but rather to collect data in place of normal heading practices. The frequency of heading (10 times) is similar to what coaches typically use, and is indeed similar to what has been reported in the prior research.

What Are the Possible Harms or Benefits?

There is no anticipated risk to you from participating in this research. However, participation in this study may cause some inconvenience to you, including:

- MRI may be dangerous for anyone with metal inside their body. Please consult Table 1. If it is not safe for you to participate, you will not be eligible to participate in the study.
- MRI is completely painless, but some people have reported minor discomforts during MRI scans (e.g. dizziness, headache/worsening headache, lightheadedness or a feeling of continued motion after being moved into the magnetic field), which usually subside within a few minutes. In rare cases, the dizziness progressed to the point of nausea, but subsided quickly outside the magnetic field.
- Up to 37% of persons undergoing MRI report moderate to severe levels of stress or anxiety and between 1% and 6% request that the procedure be discontinued due to onset of severe stress, anxiety or panic attacks. In extremely rare cases this feeling seems to have triggered a more persistent claustrophobia.
- It is possible that an improper heading technique could result in the ball impacting other parts of the body and/or increase your risk of concussion.

Please let us know immediately if you experience any discomfort, and we will discontinue the study.

Please note that MRI does not use ionizing radiation and there is no safety risk related to radiation exposure in this study. No long-term adverse effects of MRI have been reported. We will contact you if any new risks are discovered during this study. Please contact us or ask your physician to do so if you experience any effects that you feel may be a result of your participation in the study.

It is likely that you **will not directly benefit** by participating in this brain-scanning study.

Notably, your choice to participate (or not) would have no impact on your health care or your ability to continue to play soccer and other sports.

Incidental Findings

In approximately 1-5% of MRI research scans on healthy volunteers, a researcher sees something that suggests the presence of a medical condition. If a medical question arises in your case, the researcher will contact a medical specialist (i.e., radiologist) to review your scan. If the specialist decides that there is no indication of a problem, nothing further will be done. If the specialist decides that further medical follow-up should be considered, your family doctor (i.e., general practitioner) will be contacted. Please note your MRI will not be released to the physician.

For this reason that we ask you to provide us with the name of your family doctor (i.e., general practitioner) in the unlikely event that it will be needed. If you are not willing to provide the name of your doctor, we will not be able to include you in this study.

For some people, medical investigations can be upsetting, and for some, the existence of a diagnostic investigation (however it turns out) can affect insurance coverage. You should not take part in this research if you do not wish to risk the possibility of further medical investigation.

You Have the Right to Change your Mind

You have the right to withdraw from the research study at any time and for *any* reason. The research team reserve the right to end your participation for any reason.

Your participation in this research must be completely voluntary. If you do decide to participate, you may withdraw at any time without any consequences or any explanation. If you do withdraw from the study, all of your data will be destroyed and will not be used in the analysis.

To make sure that your participation continues to be voluntary, we will go through the consent procedure with you each time you participate in the study. You can choose not to participate at any time.

Is the Study Confidential?

The following standards for confidentiality will be used:

- All data obtained during your scans will be stored with a code instead of your name. Only your file, which will be kept in a locked cabinet, will have information, which relates your name to the code. Data from this study will be disposed of at least 7 years after the completion of the study; at this time, electronic data will be erased and paper copies will be shredded.

- Data transferred from West Coast Medical Imaging via an external hard drive to the University of Victoria to be kept as detailed above.

The following exceptions to confidentiality apply in your case:

Organizations that may inspect and / or copy your research results for quality assurance and data analysis include groups such as the:

- University of Victoria Research Ethics Board

Information gathered in this research study may be published or presented in public forums. Your name will not be used or revealed in such presentations. Although studies will note that data were collected on youth soccer players in Victoria, BC, information in the studies (e.g., brain scans) cannot be linked to you personally.

What will happen with the results?

Please note, group level results may be used as part of graduate theses or dissertation work and may be further disseminated at research conferences or publications. No identifying, individual data will be released. Your anonymous data may be used for future analyses in future research projects.

How Can I Get More Information?

To receive additional information from the researchers, or to learn about the results of the study (when completed) please contact any one of the research team by email or phone using the contact information provided on page 1.

In addition to being able to contact the researcher at the above phone numbers, you may verify the ethical approval of this study, or raise any concerns you might have, by contacting:

- The Human Research Ethics Office at the University of Victoria: phone 250-370-8620; email: ethics@uvic.ca

Scan 1: Signatures

The Effect of Multiple Sub-Concussive Impacts during Heading in Soccer on Brain Structure and Function

- I have received a copy of and I have read this Consent Form. I understand the nature of the study, including the potential risks and benefits. I have had adequate time to consider the information. My questions about the study have been answered.
- I will be given a copy of this document, after signing it.
- By signing this document I am not waiving any legal rights. I hereby agree to participate in the study. My consent has been freely given.

In case of a possible abnormality showing up on the MR scan, I wish my doctor,
Dr., to be informed.

I give permission to disclose information to the physician I have named for the purpose of follow-up.

* If you do not have a family physician, please list a nurse practitioner or drop-in clinic. *

By checking this box, I agree to the use of my anonymous data in future analyses/studies

Your signature below indicates that you understand the above conditions of participation in this study and that you have had the opportunity to have your questions answered by the researchers.

Name of Participant

Signature

Date

Guardian of Participant

Signature

Date

A copy of this consent will be left with you, and a copy will be taken by the researcher.

Heading Practice: Signatures

The Effect of Multiple Sub-Concussive Impacts during Heading in Soccer on Brain Structure and Function

- I have received a copy of and I have read this Consent Form. I understand the nature of the study, including the potential risks and benefits. I have had adequate time to consider the information. My questions about the study have been answered.
- I will be given a copy of this document, after signing it.
- By signing this document I am not waiving any legal rights. I hereby agree to participate in the study. My consent has been freely given.

Your signature below indicates that you understand the above conditions of participation in this study and that you have had the opportunity to have your questions answered by the researchers.

Name of Participant

Signature

Date

Guardian of Participant

Signature

Date

A copy of this consent will be left with you, and a copy will be taken by the researcher

Scan 2: Signatures

The Effect of Multiple Sub-Concussive Impacts during Heading in Soccer on Brain Structure and Function

- I have received a copy of and I have read this Consent Form. I understand the nature of the study, including the potential risks and benefits. I have had adequate time to consider the information. My questions about the study have been answered.
- I will be given a copy of this document, after signing it.
- By signing this document I am not waiving any legal rights. I hereby agree to participate in the study. My consent has been freely given.

In case of a possible abnormality showing up on the MR scan, I wish my doctor,
Dr., to be informed.
I give permission to disclose information to the physician I have named for the purpose of
follow-up.
* If you do not have a family physician, please list a nurse practitioner or drop-in clinic. *

By checking this box, I agree to the use of my anonymous data in future analyses/studies

Your signature below indicates that you understand the above conditions of participation in this study and that you have had the opportunity to have your questions answered by the researchers.

Name of Participant

Signature

Date

Guardian of Participant

Signature

Date

A copy of this consent will be left with you, and a copy will be taken by the researcher.

PARTICIPANT NUMBER: _____

Division of Medical Sciences
University of Victoria

Participant Consent Form

The Vancouver Island Concussion Project – The Effect of Sub-Concussive Impact During Repetitive Heading in Soccer Practices on Heart Rate Variability and Cognition

Participants Selection

You have been invited to participate in a study entitled the “Vancouver Island Concussion Project –The Effect of Sub-Concussive Impact During Repetitive Heading in Soccer Practices on Heart Rate Variability and Cognition” that is being conducted by Project Coordinator Rebecca Kenny and Samantha Kennedy. You are being asked to participate in this study because you are a youth soccer athlete between 13-25 years of age and have previous experience heading in soccer. Please note that participation is voluntary, you are under no obligation to participate in this study, and may withdraw from the study at any time.

Rebecca Kenny is a Graduate Students at the University of Victoria. Samantha Kennedy is a medical school student. This research is under the co-supervision of Dr. Brian Christie and Dr. Lynne Stuart-Hill.

Purpose and Objectives

The purpose of this research is to determine if repetitive, intentional heading causes sub-concussive effects. Sub-concussive impacts are contacts to the head from other players, the ball, the ground, etc. that do not cause the typical concussive symptoms, but still may cause changes to the brain. Heading is an important part of soccer, yet recent research has indicated that repetitive heading may cause sub-concussive injury. This type of repetitive injury may be dangerous, especially to the developing brain. The United States Soccer Federation recently released recommendations decreasing the amount of heading in youth soccer.

Even with the recent changes to heading regulations, the current body of research lacks consensus. Most studies attempt to correlate between changes in cognition pre/post season or game and frequency of heading during the season or game. Little research has been done investigating repetitive, intentional heading in soccer practices. Additionally, few studies have investigated sub-concussive injuries using a physiological measure.

In this project, the effects of repetitive, intentional heading during a soccer practice on heart rate variability (HRV) and cognition in youth soccer athletes will be studied. Previous research has determined that changes to HRV occur after brain injury, including concussions. Therefore, HRV may be used to provide real time indication that a concussive or sub-concussive injury has occurred. Participants will complete a typical heading practice while wearing heart rate monitors. Because the effects are still unknown, each day of testing will take the place of a regular soccer practice. This is to ensure that there is no additional exposure to heading by participating in this study. By comparing the results to the current standard of concussion evaluation, the SCAT-3, the ability of heart rate variability to assess sub-concussive injury and whether or not heading in practice even causes sub-concussive effects will be established.

June 4, 2016

PARTICIPANT NUMBER: _____

Importance of this Research

The main contribution of this study is to add to the current body of research investigating the potential risks of sub-concussive impacts during heading in soccer. Investigating the potential injury of heading in soccer practices in a controlled environment may assist others (coaches, parents, and soccer clubs and organizations) in making informed decisions on how to keep the game fun and safe.

What is involved?

All participants will be screened to determine eligibility prior to inclusion into the study. Part of the eligibility criteria is that participants have previous heading experience.

As a safety precaution, because the effects are still unknown, each day of testing will take the place of a regular soccer practice. This is to ensure that there is no additional exposure to heading by participating in this study.

There are no repercussions for not joining the study. Players who do not consent to testing or are ineligible will continue with their regular soccer practice.

Baseline Testing:

1. What will you do?

Baseline testing will be completed on Day 1, and will begin with Intake, PAR-Q+ and Consent forms. Information from the Intake Form will be used to determine eligibility and during data analysis. The PAR-Q+ form is solely used to determine eligibility. Participants will then wear a heart rate monitor for a series of activities:

- A baseline rest period by lying still for approximately 8 minutes.
- A steady state exercise where participants will jog at a sub-maximal, constant speed between two cones spaced 20m apart.
- A heading drill, that mimics a traditional heading practice.
- And then the SCAT-3. This is a cognitive test, which will require a self-report of symptoms and testing of orientation, memory, concentration, balance, reaction time, coordination and delayed recall. This cognitive data will be compared to the heart rate variability results during data analysis.

2. How long will it take?

Day 1 will take approximately 50 minutes to 1 hour.

Day 2:

1. What will you do?

Participants will be assigned to either a heading or catching group. Participants will again wear heart rate monitors to complete the following:

- A baseline rest period by lying still for approximately 8 minutes.
- A heading drill, that mimics a traditional heading practice.
- A post-exercise rest period by lying still for approximately 8 minutes.
- The same steady state exercise as described above.
- And then the SCAT-3 cognitive test.

2. How long will it take?

June 4, 2016

PARTICIPANT NUMBER: _____

Testing should take between 50 minutes to 1 hour.

Inconvenience

Participation in this study should cause little inconvenience to you/your child. However, we are asking for you to schedule time for you/your child to be tested, which may cause a slight inconvenience to you/your child.

Risks

With this research there are known risks with participation. However, these risks are deemed minimal as they are the same risks that are present in regular practices/games. Participants may experience physical and mental fatigue following the cognitive and or sub-maximal exercise tests. Participants may also experience physical injury and/or risk of concussion (e.g. muscle strain or ball impact) during the sub-maximal tests or heading/catching drills.

If possible injury does occur, the activity will be terminated and the participant's guardian(s) will be notified. There will be at least one researcher with valid First-Aid and CPR-C present at all times. If the participant experiences concussive symptoms, a SCAT-3 cognitive test will be performed. The SCAT-3 test is currently the gold-standard test for sideline concussion assessments. Medical professionals can compare post-injury and baseline SCAT-3 scores to aid in diagnosis. The post-injury SCAT-3 test along with the baseline will be provided to the participant's guardians, which can then be given to the medical professional of their choice.

Benefits

Head injuries are common in children, youth and athlete populations, and as such are a major public health concern. Establishing best practice guidelines developed through research is important. The outcome of this study has the potential to inform parents, coaches, and soccer organizations if current soccer heading drills affect players' physiology. The results could be used to determine if new protocols are necessary to ensure youth safety in soccer. This research focuses on validating physiological tools such as HRV that may help provide more sensitive measurement of sub-concussive impacts during real-time. This work will potentially generate knowledge on the degree of injury sustained by sub-concussive impact.

While participation in the study would increase the current research on the topic of potential concussive or sub-concussive injury while heading, it is unlikely that there are will be any direct benefits to participants.

Voluntary Participation

Your participation in this research must be completely voluntary. If you participate, you may withdraw at any time without any consequences or any explanation. If you withdraw, study data will be used only if you give permission.

On-going Consent

To make sure that you continue to consent to participate in this research, we will schedule all

June 4, 2016

PARTICIPANT NUMBER: _____

appointments well in advance and provide you with a summary of dates and times. You will initial and date an on-going consent form at the beginning of each session.

Anonymity

In terms of protecting your anonymity, a number will be assigned to you so that names will not be used. Loss of anonymity may occur due to the nature of this research in that only youth soccer players in the Victoria area will be tested. All attempts will be made to ensure your data remain anonymous.

Confidentiality

There are limits to confidentiality due to the sample size and focus group needed for this investigation (up to 40 youth soccer athletes). Due to these limits, some individuals may be able to deduce subject results. To provide a certain level of anonymity, participants will be assigned a number. Only participant numbers will be used when analyzing and presenting data.

Your confidentiality and the confidentiality of the data will be protected by storing all data in a password protected excel file. All paperwork will be stored in a locked filing cabinet.

Please be advised that this research study includes data storage in the U.S.A through researchers' use of Google applications for data organization purposes. As such, there is a possibility that information about you that is gathered for this research study may be accessed without your knowledge or consent by the U.S. government in compliance with the U.S. Patriot Act.

Dissemination of Results

It is anticipated that the results of this study will be shared with others in the following ways:

- 1) Published articles and or book chapters;
- 2) Presentations at scholarly meetings;

Disposal of Data

All data will be kept for a minimum of 7 years to be compliant with journal publication requirements and potentially for future use on a UVic secure server.

Future Use of Data

PLEASE SELECT 1 OF THE STATEMENTS BELOW:

I consent to the use of my data in future research: _____ (Participant to provide initials)

I **do not** consent to the use of my data in future research: _____ (Participant to provide initials)

I consent to be contacted in the event my data is requested for future research: _____ (Participant to provide initials)

June 4, 2016

PARTICIPANT NUMBER: _____

In addition, you may verify the ethical approval of this study, or raise any concerns you might have, by contacting the Human Research Ethics Office at the University of Victoria.

Your signature below indicates that you understand the above conditions of participation in this study, that you have had the opportunity to have your questions answered by the researchers, and that you give your consent for your child to participate in this research project.

Name of Participant

Signature of Participant

Date

Name of Parent/Guardian

Signature of Parent/Guardian

Date

June 4, 2016

Appendix C: MRI Pre-Screening Questionnaires

MRI PATIENT QUESTIONNAIRE

PATIENT NAME: _____	INPATIENT UNIT: _____			
PATIENT SCREENING QUESTIONS:	NO	YES	If yes, please specify	
1. Have you had a previous MRI?				
2. Have you ever been a grinder, metal worker or machinist?				
3. Have you ever, at any time, had a metallic foreign body in your eye? If yes, was it removed?				
4. Do you have any of the following:				
• cardiac pacemaker or residual wire leads?				
• artificial heart valve?				
• aneurysm clip in the brain?				
• inner ear implant?				
• electrical stimulator (for nerves or bones)? or infusion pump				
• spinal/orthopedic hardware, shrapnel, bullet?				
• any other implant in your body (penile implant, joint replacement, stents, filters)?				
• dentures, retainers, braces?				
• kidney impaired function?				
• glaucoma?				
• cardiac problems?				
• previous surgery in area being examined?				
• any surgery in the last 12 weeks?				
• Have you had injection into any joint in the last 4 weeks?				
• any mobility problems?				
5. Are you claustrophobic? If yes, extreme <input type="checkbox"/> , moderate <input type="checkbox"/> , or mild <input type="checkbox"/> ?				
6. Women: Is there any chance that you are pregnant?				
7. Do you have any allergies?				
Patient height _____	Patient weight _____			
Physician / Nurse Signature		Patient Signature		

Appendix D: Participant Intake Form

*Assessors will fill out the top section

Group		Participant Number	
DOB (yyyy/mm/dd)		Gender	
Date (yyyy/mm/dd/time)		Header or Catcher	

MOT AND RELATED TESTING – INTAKE FORM

CONTACT INFORMATION			
First Name		Last Name	
Phone (home)		Phone (cell)	
Email			

EMERGENCY CONTACT INFORMATION			
First Name		Last Name	
Phone (home)		Phone (cell)	
Email			
Relationship to You			

GENERAL INFORMATION			
Height (ft)		Weight (lbs)	
Age		DOB (yyyy/mm/dd)	
Gender		Highest Education Level	
What hand do you write with?		What foot do you shoot with?	

NUTRITION AND HEALTH	
1.	Have you been diagnosed with allergies or asthma? YES / NO
2.	Have you been diagnosed with diabetes? YES / NO

Are you on any medications? If yes, please list:

Do you have any neck/other injuries that have prevented you from participating in your regular soccer practices? if yes, please list:

CURRENT SPORT PARTICIPATION			
SPORT	POSITION	LEVEL	YEARS
Soccer			

CONCUSSION HISTORY	
Have you ever had a concussion?	
Date of most recent concussion (yyyy/mm/dd)	
How many concussions have you had in total?	

SPECIFIC CONCUSSION HISTORY				
Date of Concussion (yyyy/mm/dd)	Did you lose consciousness?	Were you playing sport?	Did you see a Doctor?	How long did it take to Return to Play?

SPECIFIC HEADING HISTORY (estimate as best you can)				
What age did you start Heading in practices?	What age did you start Heading in games?	How many headers did you do per week during practice this season?	How many headers did you do per game this season?	Do you wear any protective head-gear/bands?

NOTES

Appendix E: Medical History Form

Date of Testing: _____ Day: _____ Month: _____ Year: _____

Participant Number (*provided by researcher*): _____

Age: _____ Gender: M F Height (in feet and inches): _____ Weight (in pounds): _____

Handedness: Right Left Country of Origin: _____

Do you have normal/corrected vision? Yes No

Do you have normal hearing? Yes No

Has a professional ever diagnosed you with a Traumatic Brain Injury (not including a concussion)? Yes No

Has a physician ever diagnosed you with any neurological conditions (e.g., epilepsy)?
Yes No

Previous Diagnoses? (Please circle all that apply)

Attention Deficit Hyperactivity Disorder	Yes	No
Fetal Alcohol Syndrome Disorder	Yes	No
Autism	Yes	No
Any Other Developmental Disorder Please specify:	Yes	No
Learning Disorder/Disability Please specify:	Yes	No
Have you ever received learning assistance or extra accommodations at school? In what areas (e.g. Math, Reading, Writing)?	Yes	No
Have you ever had any speech/language difficulties?	Yes	No
Any Psychological Conditions? Please Specify:	Yes	No

Are you currently taking any prescription medication? Yes No

- If YES, which type of medication:
- How often do you take it:
- How much do you take each time:

Have you consumed any alcohol in the past 48 hours? Yes No

- Please Specify approximately how much:

Athletic History

Do you compete in a sport (e.g., soccer, rugby, etc.)? Y N

If yes, please name the sport(s) in which you compete. (You can report up to three sports).

	Sport 1	Sport 2	Sport 3
Name of Sport			
At what level do you compete in this sport (circle one)?	Recreation Club Interuniversity Professional Other, specify:	Recreation Club Interuniversity Professional Other, specify:	Recreation Club Interuniversity Professional Other, specify:
What position do you play in your sport?			
How many years have you competed in this sport at any competitive level?			
Are you currently in a season of competition for this sport?	Y N	Y N	Y N
In a typical training week (i.e., 7 days), how many hours do you practice for this sport?			

Physical Activity

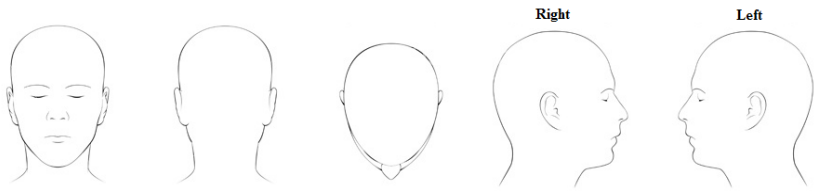
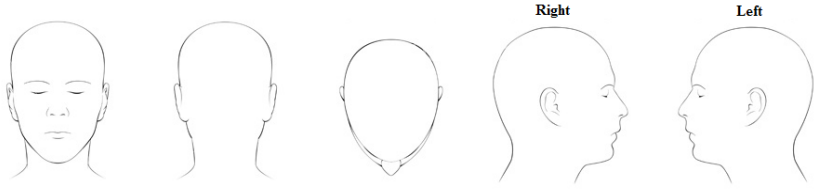
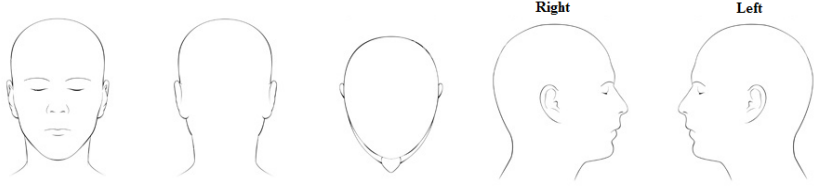
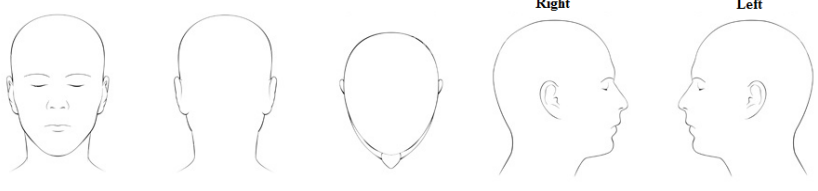
During a typical seven-day period (a week), how many times on the average do you do the following kinds of exercise for more than 15 minutes during your free time (write on each line the appropriate number).	
A) STRENUOUS EXERCISE (Heart beats rapidly, e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling)	Time per Week _____
B) MODERATE EXERCISE (Not exhausting, e.g., hiking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)	Time per Week _____
C) MILD EXERCISE (Minimal effort, e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snowmobiling, easy walking)	Time per Week _____
During a typical seven-day period (a week), in your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?	<u>Please check one</u> Often _____ Sometimes _____ Rarely/Never _____
During the last four weeks, how many minutes per week did you participate in exercise or physical activity?	<u>Please check one</u> < 30 minutes _____ 21-40 minutes _____ 41-60 minutes _____ 61-90 minutes _____ 91-120 minutes _____ > 121 minutes _____

Concussion History (if you are unsure, please circle N)

	Concussion 1 (Most Recent)	Concussion 2	Concussion 3	Concussion 4 (Least Recent)
Was this concussion diagnosed by a professional (e.g., doctor, certified athletic trainer, etc.)?	Y N	Y N	Y N	Y N
When did you experience this concussion?	Day: Month: Year:	Day: Month: Year:	Day: Month: Year:	Day: Month: Year:
Was this concussion sports-related (i.e., occurred during an athletic event)?	Y N	Y N	Y N	Y N
If sports-related, in which sport did it occur?				
Did you lose consciousness as a result of this concussion?	Y N	Y N	Y N	Y N
Did your concussion result from a head impact?	Y N	Y N	Y N	Y N
Were you wearing a helmet?	Y N	Y N	Y N	Y N
Did you experience any of the below symptoms as a result of this concussion?				
Headache	Y N	Y N	Y N	Y N
Dizziness or vertigo	Y N	Y N	Y N	Y N
Lack of awareness of surroundings	Y N	Y N	Y N	Y N
Nausea or vomiting	Y N	Y N	Y N	Y N
Light-headedness	Y N	Y N	Y N	Y N
Poor attention and concentration	Y N	Y N	Y N	Y N
Memory problems	Y N	Y N	Y N	Y N
Becoming easily fatigued	Y N	Y N	Y N	Y N
Irritable	Y N	Y N	Y N	Y N

Sensitivity to bright lights	Y N	Y N	Y N	Y N
Sensitivity to loud noises	Y N	Y N	Y N	Y N
If you had any of these symptoms, did they last over 15 mins?	Y N	Y N	Y N	Y N

For each concussion you reported on the previous page, circle where the head impact occurred on the diagram below. If the concussion did not occur due to a head impact or you are unsure about the location of impact, leave the diagram blank.

Concussion 1	
Concussion 2	
Concussion 3	
Concussion 4	

Appendix F: PAR-Q Form

CSEP approved Sept 12 2011 version

PAR-Q+

The Physical Activity Readiness Questionnaire for Everyone

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

SECTION 1 - GENERAL HEALTH

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

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



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

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



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



Delay becoming more active if:

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

SECTION 2 - CHRONIC MEDICAL CONDITIONS

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

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

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

PAR-Q+



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

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



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

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



Delay becoming more active if:

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

SECTION 3 - DECLARATION

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

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

NAME _____ DATE _____

SIGNATURE _____ WITNESS _____

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER _____

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

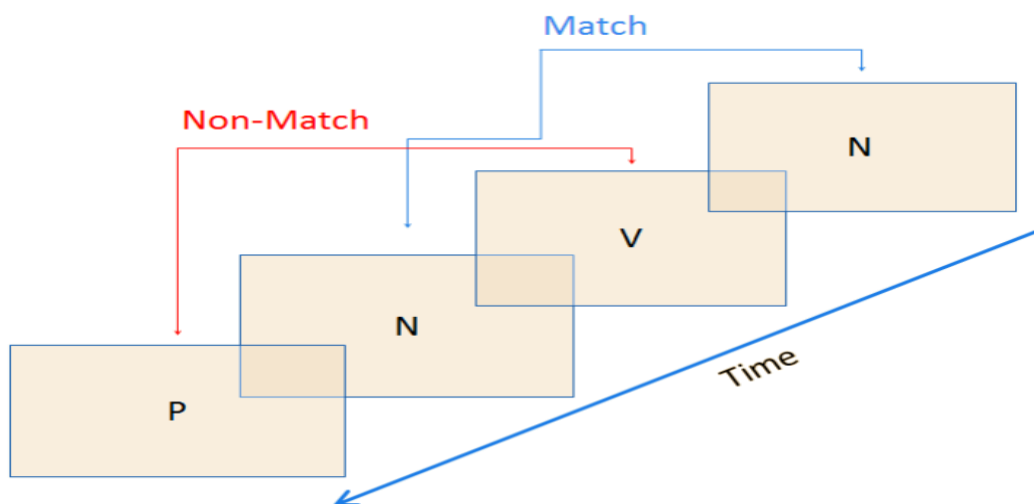
KEY REFERENCES

1. Jamnik VJ, Warburton DER, Makarski J, McKenzie DC, Shephard RJ, Stone J, and Gledhill N. Enhancing the effectiveness of clearance for physical activity participation; background and overall process. APNM 36(51):S3-S13, 2011.
2. Warburton DER, Gledhill N, Jamnik VK, Bredin SSD, McKenzie DC, Stone J, Charlesworth S, and Shephard RJ. Evidence-based risk assessment and recommendations for physical activity clearance; Consensus Document. APNM 36(51):S266-s298, 2011.

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

Appendix G: Behavioural Task Descriptions

1. The n-back task is a commonly used measure of working memory capacity (Berti, 2008). The test is designed to demonstrate how adept subjects are at updating, holding, and discarding information. Participants are shown a series of letters one at a time at a computer. Participants will indicate when the current letter matches the letter shown either 1 (easy) or 3 (difficult) trials prior. There will be 4 blocks of and a total of 150 trials. Between each trial a blank screen is shown for 1.5 seconds, and total time for the task is approximately 6 minutes.



2. To examine shifting ability, participants will complete a *More Than/Less Than* Task (i.e., deciding whether a digit is more or less than 5) and an *Odd/Even* Task (i.e., deciding whether a digit is odd or even; Friedman, Nessler, Johnson, Ritter, & Bersick, 2007). Both tasks will consist of multiple trials involving a single white digit displayed on a black background. A new digit will appear for each successive trial, with the digit displayed on the screen until the participant provides a response. After a response, the participants will wait 500 ms until seeing the successive digit. Depending on the task, the words "more less" or "odd even" will be displayed below the digit to prompt the participants regarding task instructions. These two tasks comprised the full shifting condition, which will consist of six total blocks. The first two blocks will have participants perform the same task (i.e., either all *More/Less* or all *Odd/Even*). The third to sixth blocks will include 10 task-switch trials, requiring participants to switch from one task to another when a white rectangle surrounds the displayed number. Switch trials will occur randomly, with a minimum of 7 to 13 non-switch trials in between each switch. This task takes about 6 minutes to complete.

7

Even or Odd?

3. To assess each participant's level of inhibitory processing, the Go/No-Go task will be used to measure prepotent response inhibition (Heil et al., 2000). The task will consist of two blocks of 50 and 150 trials, respectively; in the first block, participants are asked to respond as quickly as possible to any letter appearing in the centre of the computer screen by pressing the spacebar (i.e., in the "go" condition all trials are "go" trials) to create baseline reaction times. In the second block, participants are asked to do as they did in the first block, except that they are to refrain from responding when the letter j (the target stimulus) appears (i.e., the "no go" trials in the "no go" condition). Between 30-35% of the trials in the "no go" condition are "no go" trials. Inter-trial interval time is variable at approximately 1400 ms average, and task completion time is approximately 6 minutes.

Appendix H: Heart Rate Variability Assessment Instructions

Day 1 (~ 45 minutes)

- Remember to note start and end times!
1. Confirm Informed Consent and PAR-Q+ eligibility
 - If participant and parent have not completed consent, they must do so before starting testing.
 - When completing the PAR-Q+, tester cannot answer any questions for the participant. The tester may clarify questions, but the participant must complete the final "yes"/"no" answer.
 - If participant answers "yes" to any questions in Sections 1 and 2, they must be cleared by a doctor before participating in testing.
 2. Fill out the Intake Form
 3. Have participant put on the heart rate monitor
 - Water or electrode gel must be placed on the electrodes of the monitor.
 - Participant places monitor under shirt, around their chest.
 - Before beginning testing, ensure that the heart rate monitor is picking up a heart beat (look for the flashing red heart on the monitor). Continually check this connection throughout testing.
 4. Baseline rest for 8 minutes
 - Participant lies COMPLETELY still on the mat with eyes closed for 8 minutes.
 - If the participant moves, remind them to stay still and continue with the 8 minutes of rest.
 - Testers should be watching to ensure the participants are staying still.
 5. Catching: 2 sets of 5 (10 total in around 5 minutes)
 - Participants stand 12ft (3.65m) away from each other. One participant will throw the ball 5 times, while the other will head it back or catch it. The participants will then switch roles between throwing and heading/catching, and keep switching until each participant has completed 10 headers/catches.
 - If heading, participants must keep both feet on the ground (i.e. no jumping), and hit the ball with the front of their head, aiming it towards the thrower.
 - If catching, participants should catch the ball at face height.
 - Keep track of the start/end times and number of headers/catches.
 - If participants exhibit/complain of concussive symptoms after completing the heading protocol, complete a SCAT3 cognitive assessment right away to compare to their baseline SCAT3. Participant may be withdrawn from completing testing.
 6. Rest for 8 minutes
 - Participants will complete another 8 minutes of rest as before (see above).
 7. Steady state exercise
 - Set up two cones 65.6ft (20m) apart.
 - Download the " HIIT Interval Training Timer" app, and enter the following settings:
 - Prep 00:00
 - Work 00:08
 - Rest 00:00
 - Rounds 60
 - Cool down 00:00
 - Total 8:00
 - Participant runs from cone to cone for 8 minutes. They should be running at an even, steady pace, but must cross the other cone before the beep (8 seconds) (i.e. not sprinting to the cone and then resting).

- Play the tone for the participants so that they can understand how much time they have to reach the cone. Testers should run the first few laps with participants to ensure that they are maintaining a steady pace.
 - Testers should be watching for participants not maintaining the steady pace (i.e. reaching the cones too early or too late), and provide participants with feedback if they are not meeting the requirements.
5. SCAT3 Cognitive test
 - Complete the SCAT3 test with participants in a private and quiet area.
 - Do not complete the following sections: Glasgow coma scale, Background information, or neck examination.
 - Do complete the Maddocks score, symptoms list, cognitive assessment, balance examination, coordination examination, and SAC delayed recall.
 - To keep testing standardized, please read the script provided on the SCAT3 form.
 - Remember to get heart rate monitors from participant before they leave!

Days 2 (~ 45 minutes)

- Remember to note start and end times!
1. Confirm Informed Consent and PAR-Q+ eligibility
 - The Informed Consent and PAR-Q+ forms should have been filled out by Day 1 of testing.
 2. Fill out the Appointment History form
 - Ensure participants initial for ongoing consent and ask the additional questions.
 3. Have participant put on the heart rate monitor
 - Water or electrode gel must be placed on the electrodes of the monitor.
 - Participant places monitor under shirt, around their chest.
 - Before beginning testing, ensure that the heart rate monitor is picking up a heart beat (look for the flashing red heart on the monitor). Continually check this connection throughout testing.
 4. Baseline rest for 8 minutes
 - Participant lies COMPLETELY still on the mat with eyes closed for 8 minutes.
 - If the participant moves, remind them to stay still and continue with the 8 minutes of rest.
 - Testers should be watching to ensure the participants are staying still.
 6. Heading: 2 sets of 5 (10 total in around 5 minutes)
 - Participants stand 12ft (3.65m) away from each other. One participant will throw the ball 5 times, while the other will head it back or catch it. The participants will then switch roles between throwing and heading/catching, and keep switching until each participant has completed 10 headers/catches.
 - If heading, participants must keep both feet on the ground (i.e. no jumping), and hit the ball with the front of their head, aiming it towards the thrower.
 - If catching, participants should catch the ball at face height.
 - Keep track of the start/end times and number of headers/catches.
 - If participants exhibit/complain of concussive symptoms after completing the heading protocol, complete a SCAT3 cognitive assessment right away to compare to their baseline SCAT3 (from Day 1). Participant may be withdrawn from completing testing.
 8. Rest for 8 minutes
 - Participants will complete another 8 minutes of rest as before (see above).
 9. Steady state exercise

- Set up two cones 65.6ft (20m) apart.
 - Download the " HIIT Interval Training Timer" app, and enter the following settings:
 - Prep 00:00
 - Work 00:08
 - Rest 00:00
 - Rounds 60
 - Cool down 00:00
 - Total 8:00
 - Participant runs from cone to cone for 8 minutes. They should be running at an even, steady pace, but must cross the other cone before the beep (8 seconds) (i.e. not sprinting to the cone and then resting).
 - Play the tone for the participants so that they can understand how much time they have to reach the cone. Testers should run the first few laps with participants to ensure that they are maintaining a steady pace.
 - Testers should be watching for participants not maintaining the steady pace (i.e. reaching the cones too early or too late), and provide participants with feedback if they are not meeting the requirements.
5. SCAT3 Cognitive test
- Complete the SCAT3 test with participants in a private and quiet area.
 - Do not complete the following sections: Glasgow coma scale, Background information, or neck examination.
 - Do complete the Maddocks score, symptoms list, cognitive assessment, balance examination, coordination examination, and SAC delayed recall.
 - To keep testing standardized, please read the script provided on the SCAT3 form.
 - Remember to get heart rate monitors from participant before they leave!

Appendix I: SCAT-3 Form

SCAT3™



FIFA®



FEI

Sport Concussion Assessment Tool – 3rd Edition

For use by medical professionals only

Name

Date/Time of Injury:
Date of Assessment:

Examiner:

What is the SCAT3?¹

The SCAT3 is a standardized tool for evaluating injured athletes for concussion and can be used in athletes aged from 13 years and older. It supersedes the original SCAT and the SCAT2 published in 2005 and 2009, respectively². For younger persons, ages 12 and under, please use the Child SCAT3. The SCAT3 is designed for use by medical professionals. If you are not qualified, please use the Sport Concussion Recognition Tool³. Preseason baseline testing with the SCAT3 can be helpful for interpreting post-injury test scores.

Specific instructions for use of the SCAT3 are provided on page 3. If you are not familiar with the SCAT3, please read through these instructions carefully. This tool may be freely copied in its current form for distribution to individuals, teams, groups and organizations. Any revision or any reproduction in a digital form requires approval by the Concussion in Sport Group.

NOTE: The diagnosis of a concussion is a clinical judgment, ideally made by a medical professional. The SCAT3 should not be used solely to make, or exclude, the diagnosis of concussion in the absence of clinical judgement. An athlete may have a concussion even if their SCAT3 is "normal".

What is a concussion?

A concussion is a disturbance in brain function caused by a direct or indirect force to the head. It results in a variety of non-specific signs and/or symptoms (some examples listed below) and most often does not involve loss of consciousness. Concussion should be suspected in the presence of **any one or more** of the following:

- Symptoms (e.g., headache), or
- Physical signs (e.g., unsteadiness), or
- Impaired brain function (e.g. confusion) or
- Abnormal behaviour (e.g., change in personality).

SIDELINE ASSESSMENT

Indications for Emergency Management

NOTE: A hit to the head can sometimes be associated with a more serious brain injury. Any of the following warrants consideration of activating emergency procedures and urgent transportation to the nearest hospital:

- Glasgow Coma score less than 15
- Deteriorating mental status
- Potential spinal injury
- Progressive, worsening symptoms or new neurologic signs

Potential signs of concussion?

If any of the following signs are observed after a direct or indirect blow to the head, the athlete should stop participation, be evaluated by a medical professional and **should not be permitted to return to sport the same day** if a concussion is suspected.

Any loss of consciousness? Y N
 "If so, how long?" _____
 Balance or motor incoordination (stumbles, slow/laboured movements, etc.)? Y N
 Disorientation or confusion (inability to respond appropriately to questions)? Y N
 Loss of memory:
 "If so, how long?" _____
 "Before or after the injury?" _____
 Blank or vacant look: Y N
 Visible facial injury in combination with any of the above: Y N

1 Glasgow coma scale (GCS)

Best eye response (E)

No eye opening	1
Eye opening in response to pain	2
Eye opening to speech	3
Eyes opening spontaneously	4

Best verbal response (V)

No verbal response	1
Incomprehensible sounds	2
Inappropriate words	3
Confused	4
Oriented	5

Best motor response (M)

No motor response	1
Extension to pain	2
Abnormal flexion to pain	3
Flexion/Withdrawal to pain	4
Localizes to pain	5
Obeys commands	6

Glasgow Coma score (E + V + M) **of 15**

GCS should be recorded for all athletes in case of subsequent deterioration.

2 Maddocks Score³

"I am going to ask you a few questions, please listen carefully and give your best effort."

Modified Maddocks questions (1 point for each correct answer)

What venue are we at today?	0	1
Which half is it now?	0	1
Who scored last in this match?	0	1
What team did you play last week/game?	0	1
Did your team win the last game?	0	1

Maddocks score **of 5**

Maddocks score is validated for sideline diagnosis of concussion only and is not used for serial testing.

Notes: Mechanism of Injury ("tell me what happened?"):

Any athlete with a suspected concussion should be REMOVED FROM PLAY, medically assessed, monitored for deterioration (i.e., should not be left alone) and should not drive a motor vehicle until cleared to do so by a medical professional. No athlete diagnosed with concussion should be returned to sports participation on the day of injury.

BACKGROUND

Name: _____ Date: _____
 Examiner: _____
 Sport/team/school: _____ Date/time of injury: _____
 Age: _____ Gender: M F
 Years of education completed: _____
 Dominant hand: right left neither
 How many concussions do you think you have had in the past? _____
 When was the most recent concussion? _____
 How long was your recovery from the most recent concussion? _____
 Have you ever been hospitalized or had medical imaging done for a head injury? Y N
 Have you ever been diagnosed with headaches or migraines? Y N
 Do you have a learning disability, dyslexia, ADD/ADHD? Y N
 Have you ever been diagnosed with depression, anxiety or other psychiatric disorder? Y N
 Has anyone in your family ever been diagnosed with any of these problems? Y N
 Are you on any medications? If yes, please list: Y N

SCAT3 to be done in resting state. Best done 10 or more minutes post exercise.

SYMPTOM EVALUATION

3

How do you feel?

"You should score yourself on the following symptoms, based on how you feel now".

	none	mild	moderate	severe			
Headache	0	1	2	3	4	5	6
"Pressure in head"	0	1	2	3	4	5	6
Neck Pain	0	1	2	3	4	5	6
Nausea or vomiting	0	1	2	3	4	5	6
Dizziness	0	1	2	3	4	5	6
Blurred vision	0	1	2	3	4	5	6
Balance problems	0	1	2	3	4	5	6
Sensitivity to light	0	1	2	3	4	5	6
Sensitivity to noise	0	1	2	3	4	5	6
Feeling slowed down	0	1	2	3	4	5	6
Feeling like "in a fog"	0	1	2	3	4	5	6
"Don't feel right"	0	1	2	3	4	5	6
Difficulty concentrating	0	1	2	3	4	5	6
Difficulty remembering	0	1	2	3	4	5	6
Fatigue or low energy	0	1	2	3	4	5	6
Confusion	0	1	2	3	4	5	6
Drowsiness	0	1	2	3	4	5	6
Trouble falling asleep	0	1	2	3	4	5	6
More emotional	0	1	2	3	4	5	6
Irritability	0	1	2	3	4	5	6
Sadness	0	1	2	3	4	5	6
Nervous or Anxious	0	1	2	3	4	5	6

Total number of symptoms (Maximum possible 22) _____
 Symptom severity score (Maximum possible 132) _____

Do the symptoms get worse with physical activity? Y N
 Do the symptoms get worse with mental activity? Y N

self rated self rated and clinician monitored
 clinician interview self rated with parent input

Overall rating: If you know the athlete well prior to the injury, how different is the athlete acting compared to his/her usual self?

Please circle one response:
 no different very different unsure N/A

Scoring on the SCAT3 should not be used as a stand-alone method to diagnose concussion, measure recovery or make decisions about an athlete's readiness to return to competition after concussion. Since signs and symptoms may evolve over time, it is important to consider repeat evaluation in the acute assessment of concussion.

COGNITIVE & PHYSICAL EVALUATION

4

Cognitive assessment

Standardized Assessment of Concussion (SAC)⁴

Orientation (1 point for each correct answer)

What month is it?	0	1
What is the date today?	0	1
What is the day of the week?	0	1
What year is it?	0	1
What time is it right now? (within 1 hour)	0	1

Orientation score _____ of 5

Immediate memory

List	Trial 1	Trial 2	Trial 3	Alternative word list					
elbow	0	1	0	1	0	1	candle	baby	finger
apple	0	1	0	1	0	1	paper	monkey	penny
carpet	0	1	0	1	0	1	sugar	perfume	blanket
saddle	0	1	0	1	0	1	sandwich	sunset	lemon
bubble	0	1	0	1	0	1	wagon	iron	insect

Total _____

Immediate memory score total _____ of 15

Concentration: Digits Backward

List	Trial 1	Alternative digit list			
4-9-3	0	1	6-2-9	5-2-6	4-1-5
3-8-1-4	0	1	3-2-7-9	1-7-9-5	4-9-6-8
6-2-9-7-1	0	1	1-5-2-8-6	3-8-5-2-7	6-1-8-4-3
7-1-8-4-6-2	0	1	5-3-9-1-4-8	8-3-1-9-6-4	7-2-4-8-5-6

Total of 4 _____

Concentration: Month in Reverse Order (1 pt. for entire sequence correct)
 Dec-Nov-Oct-Sept-Aug-Jul-Jun-May-Apr-Mar-Feb-Jan 0 1
Concentration score _____ of 5

5

Neck Examination:

Range of motion _____ Tenderness _____ Upper and lower limb sensation & strength _____
Findings: _____

6

Balance examination

Do one or both of the following tests.
 Footwear (shoes, barefoot, braces, tape, etc.) _____

Modified Balance Error Scoring System (BESS) testing⁵
 Which foot was tested (i.e. which is the non-dominant foot) Left Right
 Testing surface (hard floor, field, etc.) _____

Condition

Double leg stance:	Errors
Single leg stance (non-dominant foot):	Errors
Tandem stance (non-dominant foot at back):	Errors

And/Or

Tandem gait^{6,7}
 Time (best of 4 trials): _____ seconds

7

Coordination examination

Upper limb coordination
 Which arm was tested: Left Right
Coordination score _____ of 1

8

SAC Delayed Recall⁴

Delayed recall score _____ of 5

INSTRUCTIONS

Words in *italics* throughout the SCAT3 are the instructions given to the athlete by the tester.

Symptom Scale

"You should score yourself on the following symptoms, based on how you feel now".

To be completed by the athlete. In situations where the symptom scale is being completed after exercise, it should still be done in a resting state, at least 10 minutes post exercise.

For total number of symptoms, maximum possible is 22.

For Symptom severity score, add all scores in table, maximum possible is 22 x 6 = 132.

SAC⁴

Immediate Memory

"I am going to test your memory. I will read you a list of words and when I am done, repeat back as many words as you can remember, in any order."

Trials 2 & 3:

"I am going to repeat the same list again. Repeat back as many words as you can remember in any order, even if you said the word before."

Complete all 3 trials regardless of score on trial 1 & 2. Read the words at a rate of one per second. **Score 1 pt. for each correct response.** Total score equals sum across all 3 trials. Do not inform the athlete that delayed recall will be tested.

Concentration Digits backward

"I am going to read you a string of numbers and when I am done, you repeat them back to me backwards, in reverse order of how I read them to you. For example, if I say 7-1-9, you would say 9-1-7."

If correct, go to next string length. If incorrect, read trial 2. **One point possible for each string length.** Stop after incorrect on both trials. The digits should be read at the rate of one per second.

Months in reverse order

"Now tell me the months of the year in reverse order. Start with the last month and go backward. So you'll say December, November ... Go ahead"

1 pt. for entire sequence correct

Delayed Recall

The delayed recall should be performed after completion of the Balance and Coordination Examination.

"Do you remember that list of words I read a few times earlier? Tell me as many words from the list as you can remember in any order."

Score 1 pt. for each correct response

Balance Examination

Modified Balance Error Scoring System (BESS) testing⁵

This balance testing is based on a modified version of the Balance Error Scoring System (BESS)⁵. A stopwatch or watch with a second hand is required for this testing.

"I am now going to test your balance. Please take your shoes off, roll up your pant legs above ankle (if applicable), and remove any ankle taping (if applicable). This test will consist of three twenty second tests with different stances."

(a) Double leg stance:

"The first stance is standing with your feet together with your hands on your hips and with your eyes closed. You should try to maintain stability in that position for 20 seconds. I will be counting the number of times you move out of this position. I will start timing when you are set and have closed your eyes."

(b) Single leg stance:

"If you were to kick a ball, which foot would you use? [This will be the dominant foot] Now stand on your non-dominant foot. The dominant leg should be held in approximately 30 degrees of hip flexion and 45 degrees of knee flexion. Again, you should try to maintain stability for 20 seconds with your hands on your hips and your eyes closed. I will be counting the number of times you move out of this position. If you stumble out of this position, open your eyes and return to the start position and continue balancing. I will start timing when you are set and have closed your eyes."

(c) Tandem stance:

"Now stand heel-to-toe with your non-dominant foot in back. Your weight should be evenly distributed across both feet. Again, you should try to maintain stability for 20 seconds with your hands on your hips and your eyes closed. I will be counting the number of times you move out of this position. If you stumble out of this position, open your eyes and return to the start position and continue balancing. I will start timing when you are set and have closed your eyes."

Balance testing – types of errors

1. Hands lifted off iliac crest
2. Opening eyes
3. Step, stumble, or fall
4. Moving hip into > 30 degrees abduction
5. Lifting forefoot or heel
6. Remaining out of test position > 5 sec

Each of the 20-second trials is scored by counting the errors, or deviations from the proper stance, accumulated by the athlete. The examiner will begin counting errors only after the individual has assumed the proper start position. **The modified BESS is calculated by adding one error point for each error during the three 20-second tests. The maximum total number of errors for any single condition is 10.** If a athlete commits multiple errors simultaneously, only one error is recorded but the athlete should quickly return to the testing position, and counting should resume once subject is set. Subjects that are unable to maintain the testing procedure for a minimum of **five seconds** at the start are assigned the highest possible score, ten, for that testing condition.

OPTION: For further assessment, the same 3 stances can be performed on a surface of medium density foam (e.g., approximately 50 cm x 40 cm x 6 cm).

Tandem Gait^{6,7}

Participants are instructed to stand with their feet together behind a starting line (the test is best done with footwear removed). Then, they walk in a forward direction as quickly and as accurately as possible along a 38mm wide (sports tape), 3 meter line with an alternate foot heel-to-toe gait ensuring that they approximate their heel and toe on each step. Once they cross the end of the 3m line, they turn 180 degrees and return to the starting point using the same gait. A total of 4 trials are done and the best time is retained. Athletes should complete the test in 14 seconds. Athletes fail the test if they step off the line, have a separation between their heel and toe, or if they touch or grab the examiner or an object. In this case, the time is not recorded and the trial repeated, if appropriate.

Coordination Examination

Upper limb coordination

Finger-to-nose (FTN) task:

"I am going to test your coordination now. Please sit comfortably on the chair with your eyes open and your arm (either right or left) outstretched (shoulder flexed to 90 degrees and elbow and fingers extended), pointing in front of you. When I give a start signal, I would like you to perform five successive finger to nose repetitions using your index finger to touch the tip of the nose, and then return to the starting position, as quickly and as accurately as possible."

Scoring: 5 correct repetitions in < 4 seconds = 1

Note for testers: Athletes fail the test if they do not touch their nose, do not fully extend their elbow or do not perform five repetitions. **Failure should be scored as 0.**

References & Footnotes

1. This tool has been developed by a group of international experts at the 4th International Consensus meeting on Concussion in Sport held in Zurich, Switzerland in November 2012. The full details of the conference outcomes and the authors of the tool are published in The BJSM Injury Prevention and Health Protection, 2013, Volume 47, Issue 5. The outcome paper will also be simultaneously co-published in other leading biomedical journals with the copyright held by the Concussion in Sport Group, to allow unrestricted distribution, providing no alterations are made.
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3. Maddocks, DL; Dicker, GD; Saling, MM. The assessment of orientation following concussion in athletes. Clinical Journal of Sport Medicine. 1995; 5(1): 32-3.
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6. Schneiders, A.G., Sullivan, S.J., Gray, A., Hammond-Tookey, G. & McCrory, P. Normative values for 16-37 year old subjects for three clinical measures of motor performance used in the assessment of sports concussions. Journal of Science and Medicine in Sport. 2010; 13(2): 196-201.
7. Schneiders, A.G., Sullivan, S.J., Kvarnstrom, J.K., Olsson, M., Yden, T. & Marshall, S.W. The effect of footwear and sports-surface on dynamic neurological screening in sport-related concussion. Journal of Science and Medicine in Sport. 2010; 13(4): 382-386

Appendix J: Exit Questionnaire

MRI Exit Questionnaire

Research Subject Number: _____

Protocol Number: _____

Date: _____

Thank you for participating in our study. We would appreciate it if you would answer the following questions about your experience.

	YES	NO
1) Would you participate in an MRI study again?	<input type="checkbox"/>	<input type="checkbox"/>
2) Would you like to be contacted when you are eligible for another study?	<input type="checkbox"/>	<input type="checkbox"/>
3) Was there any point in which you were tired or sleepy during the study?		

4) Please tell us how we could have made your experience more comfortable:		

5) How did you feel about the way in which you were approached about participating in this study?		

Thank you

Appendix K: Heart Rate Monitor Log

Determination of Sub-Concussive Impact during Heading in Soccer using HRV

Group		Participant Number	
DOB (yyyy/mm/dd)		Gender	

HR MONITOR LOG

Date (yyyy/mm/dd/time)		Monitor #	
Testing Day		Header or Catcher	

Test	Time on	Time off
Monitor On	00:00	--
Rest		
Heading or Catching Round 1		
Heading and Catching Round 2		
Rest		
Steady State Exercise		
SCAT3 Cognitive Test		
Monitor Off		

Appendix L: On-Going Consent and Appointment History

Group		Participant Number	
DOB (yyyy/mm/dd)		Gender	

MOT AND RELATED TESTING – APPOINTMENT HISTORY AND ON-GOING CONSENT

Date (yyyy/mm/dd)	Participant Initial	Header or Catcher	Heading	Daily questions	Notes
			<p><u>Sample: Throws #7&9 were headed improperly. Throw #4 lead to no head contact, therefore, 11 throws were completed. 10 head contacts in total.</u></p> <p><u>Proper: 1,2,3,5,6,8,9,10,11</u></p> <p><u>Improper: 7,9</u></p> <p><u>No contact: 4</u></p>	<ul style="list-style-type: none"> • Have you had any caffeine rich beverages/energy drinks in the last hour? YES / NO • Do you have any cold symptoms? YES / NO 	<p>if yes to cold symptoms, describe:</p>
			<p><u>Proper:</u></p> <p><u>Improper:</u></p> <p><u>No contact:</u></p>	<ul style="list-style-type: none"> • Have you had any caffeine rich beverages/energy drinks in the last hour? YES / NO • Do you have any cold symptoms? YES / NO 	<p>if yes to cold symptoms, describe:</p>
			<p><u>Proper:</u></p> <p><u>Improper:</u></p> <p><u>No contact:</u></p>	<ul style="list-style-type: none"> • Have you had any caffeine rich beverages/energy drinks in the last hour? YES / NO • Do you have any cold symptoms? YES / NO 	<p>if yes to cold symptoms, describe:</p>