Head impact severity associated with loss of consciousness and impact seizures in sport-related concussions

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"Never say never because limits, like fears, are often just an illusion"

Michael Jordan

Abstract

The severity of injury associated with sport concussions that present with a loss of consciousness or impact seizures is ambiguous. A disconnect between the clinical and biomechanical aspect can be observed throughout the literature pertaining to loss of consciousness and impact seizures. Clinicians have dismissed a loss of consciousness or the presence of impact seizures as an indicator of severity. However, early biomechanical research suggests that loss of consciousness is caused by greater magnitudes of impacts and damage to more vulnerable brain regions. However, this research was conducted on animal and cadaver models and may not adequately represent sport-related concussions. Recent methodologies such as laboratory reconstructions of head impacts and finite element modeling can provide new information on the severity of impact associated with these signs of concussions.

Study One compared the magnitudes of head dynamic response and brain tissue deformation between impact representations of punches that lead or do not lead to LOC in boxing. The main findings of this study revealed knockout punches were the result of by unprotected hooks to the mandibular angle resulting in greater brain tissue trauma.

Study Two compared cases of concussions with and without LOC in American football. Head dynamic response and brain tissue deformation was also greater in the LOC group in this sport, consistent with boxing impacts. The main predictor of LOC was found to be impact velocity which has implications in terms of prevention.

Study Three compared the magnitudes of head dynamic response and brain tissue deformation between cases of concussions with a loss of consciousness and cases of concussion with impact seizures in American football. The two types of clinical presentations had similar severities of brain tissue deformation with the exception of strain rate in the white matter being smaller in cases of impact seizures.

The findings of this thesis support the notion that concussions with loss of consciousness or impact seizure represent a more severe injury than concussions without these signs. It may be appropriate to address these signs of injury differently in return to sport protocols to reflect their severity. The findings also suggests that prevention of loss of consciousness should be sport specific. Hooks to the side of the jaw were the primary cause in boxing, whereas LOC could be caused by different event types in American football. However, in both sports, impact velocity and impact location played an important role in the risk for loss of consciousness.

Preface

This thesis dissertation is organized in three parts:

I. Introduction, which introduces the background, the research questions, the literature review and the thesis objectives

II. Severity of impacts associated with loss of consciousness and impact seizures which consist of three studies that aim to answer the research question: Are head impacts with loss of consciousness or impact seizures associated with higher magnitudes of head kinematic and brain tissue deformation than head impacts without these signs?

III. Closing which provides discussion, implications of the findings and limitations of the present research

This doctoral dissertation includes three original articles for which I was responsible for and fully participated in:

1) the conception and design of the studies;
2) data acquisition, analysis and interpretation;
3) drafting, revising, and submission of the articles for peer review in scholarly journals.

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PART I

1. Background

Sports concussions can result in debilitating consequences such as persistent post-concussion syndrome (PCS), depression, and cognitive impairment (Guskiewicz, et al., 2005; Guskiewics, et al., 2007). Multiple researchers have sought to help predict these consequences, but the factors influencing poor outcomes are not well understood. One of the most researched variables involves the loss of consciousness (LOC). In the past, LOC used to be the hallmark sign of concussion. Several definitions described concussions as loss of consciousness due to head impacts (Ward, 1966; Walker, 1973; Ommaya & Gennarelli, 1974). When the definition evolved to include other signs and symptoms, LOC became an indicator of severity. A number of grading scales were developed and were characterized by LOC resulting in a more severe grade of injury (Cantu, 2001). Health care professionals were advised to delay the return to play of an athlete who had sustained a loss of consciousness (Cantu, 2001). Currently, less emphasis is put on LOC as an indicator of severity. LOC is simply a red flag prompting an athlete to be sent to the emergency department to rule out a more severe injury (McCrory, et al., 2017). Once it is established that there is no severe traumatic brain injury, the athlete enters the same return to play protocol as athletes who have not lost consciousness.

The role of abnormal motor responses such as impact seizures (figure 1) in the determination of severity of concussive injury has also shifted over the years. Similar types of motor responses have been reported to be associated with 66% of head impacts with loss of consciousness (Hosseini & Lifshitz, 2009). Impact seizures are currently not considered an indicator of injury severity but were considered as a sign of a complex concussions in the past (McCrory, et al., 2005). To the author's knowledge, only one concussion protocol currently specifically addresses impact seizures. The National Football League (NFL) recently announced that they were now treating impact seizures in the same manner as LOC, namely as an indicator that an athlete needs to be removed from the game, evaluated and not allowed to return on the field on the same day (Ellenbogen, et al., 2018) [Appendix B1]. Impact seizures have been described in the literature as abnormal posturing, fencing response, or concussive convulsions (Hosseini & Lifshitz, 2009; McCrory & Berkovic, 1998; Bricolo, Turazzi, Alexandre, & Rizzuto, 1977), which can be confusing. In order to keep this thesis clear and concise, the term impact seizures will be used to stay consistent with the description used by the NFL. Exceptions will be made when referring to previous research.

Figure 1. *Impact seizures from a fall in an American football player. Figure found on si.com*

The science behind the decisions of not considering LOC and impact seizures as an indicator of injury severity was predominantly based on outcomes such as recovery time and performance on neuropsychological tests. These outcomes are influenced by other factors such as anxiety, coping mechanisms and individual differences (Collie, Darby, & Maruff, 2001), which can make conclusions in terms of severity challenging. The severity of the impact and the resulting brain trauma were not investigated and therefore were never considered when changes in return to sports protocols were made. In addition, a better understanding of the impact characteristics associated with loss of consciousness is needed to develop better prevention strategies.

Laboratory reconstruction of head impacts and finite element modeling provide information on the severity of head impacts by describing the magnitudes of brain tissue trauma associated with impacts causing a loss of consciousness and impact seizures, and provide a better understanding of the biomechanical factors contributing to the risk of an athlete to experience these clinical signs. This thesis is designed to further the knowledge on the severity of loss of consciousness and impact seizures in sports by characterizing the magnitudes of head dynamic response and brain tissue trauma associated with these signs of concussions.

2. Sports associated with loss of consciousness and impact seizures

Boxing

All contact sports have a potential risk for concussions with a loss of consciousness or impact seizures. Boxing was selected for this thesis because the objective of a boxing match is to knock-out the opponent. Eleven percent of boxing matches are decided by KO or TKO making it an ideal sport to study loss of consciousness (Bledsoe, Li, & Levy, 2005). Anecdotally, boxers report that a knock-out is more likely to occur by a hook to the side of the jaw. This is consistent with biomechanical studies that have demonstrated that hooks induce a greater amount of head acceleration, particularly rotational acceleration (Stojsih, Boitano, Whilelm, & Bir, 2008; Viano D. , et al., 2005b), the proposed mechanism of LOC (Ommaya & Hirsh, 1971b; Gennarelli, Thibault, & Ommaya, 1971). Although there have been multiple studies examining head biomechanics from boxing punches (Walilko, Viano, & Bir, 2005; Viano D. , et al., 2005b; Stojsih, Boitano, Whilelm, & Bir, 2008), none has investigated the difference in magnitudes brain tissue deformation between punches that lead to LOC and those that do not.

American football

American football impacts deliver high levels of energy that result in a high incidence of concussive injuries. Loss of consciousness and impact seizures are sometimes observed in conjunction with these injuries making American football another suitable sport for the examination of the severity of impacts associated with loss of consciousness and impact seizures.

LOC occurs in association with eight percent of reported concussion cases in the NFL (Casson, Viano, & Pellman, 2010) with other researchers reporting greater incidence of LOC in high school football. Collins et al. (2003) examined a sample of 78 concussed athletes and reported that 19.2% of athletes sustained a loss of consciousness. Lau et al. (2011) reported an incidence of LOC of 13.3% of loss of consciousness in high school football players who had sustained a concussion. The incidence of impact seizures in American football is not reported.

Contrary to boxing, LOC in American football can be induced by multiple events such as falls, helmet-to-helmet collisions and shoulder-to-helmet collisions. These events result in different curve shapes of head acceleration and may not exhibit similar brain tissue distribution (Kendall, 2016). This suggests that LOC and impact seizures may be caused by different mechanisms or different impact characteristics depending on the type of event that induced the response. This is important to understand in order to design effective sport-specific prevention strategies.

3. Loss of consciousness and impact seizures as indicators of severity

Loss of consciousness and recovery time

There is no consensus regarding whether loss of consciousness can help predict a delayed recovery after a concussion. Bazarian and colleagues (1999) investigated if LOC could predict PCS at one, three and sixth month after the injury in an emergency population. They reported that the duration of LOC could predict PCS at all three time intervals, and that the presence of LOC could predict PCS at three months. Casson et al. (2010) reported that the presence of LOC (n=57) resulted in a greater likelihood of not returning to the game within a week when compared to players who had not lost consciousness. Benson et al (2011) showed that hockey players who had lost consciousness were more likely to have recovery times longer than 10 days. McCrea et al. (2013) also reported that high school and collegiate athletes with LOC were slower to recover. In contrast, Lau et al. (2009) found that loss of consciousness was not associated with delayed return to play in a sample of high school football players. However, their sample only included 13 athletes who had lost consciousness. This small sample size may have influenced why the results of the logistic regression were not significant.

Loss of consciousness and performance on neuropsychological tests and cognitive functions

Several researchers have investigated the influence of LOC on neuropsychological performance. The vast majority reports no influence of LOC on the results of the tests. Only one paper reported that subjects with a loss of consciousness from motor vehicle accidents had greater impairments on speed dependent tests as well as verbal memory and delayed recall (Hickling, Gillen, Blanchard, Buckley, & Taylor, 1998). Other researchers describe no association between LOC and poor performance on neuropsychological tests. Leininger et al. (1990) found no differences on the score of eight neuropsychological tests in a population principally composed of motor vehicle accident victims. It would be important to note that these tests were performed within an interval ranging from one month to 22 months post-injury and may have influenced the findings. In a similar population, Lovell et al. (1999) reported that subjects who had experienced LOC did not have a significantly poorer performance on eight neuropsychological tests. Iverson et al. (2000) investigated whether LOC had an effect on cognitive functioning after a mild head injury and showed that patients who had lost consciousness did not differ from non-LOC patients in terms of attention, learning, memory, language, and executive functioning. Similar results were found in the athletic population. Collins et al. (2003) and Lau et al. (2009) reported that athletes who lost consciousness did not perform worse on neuropsychological tests than athletes who did not. Again, the sample sizes of the LOC groups were small (15.9% and 11.2% of the total study population respectively).

Impact seizures and severity of injury

The majority of evidence on the relationship between impact seizures and the severity of concussive injury involved Australian rules football and rugby. McCrory and colleagues (1997) reported that the 22 cases of concussive convulsions that they observed did not result in structural abnormalities on neuroimaging, nor in deficits in neuropsychological testing. Additionally, every subjects returned to full participation in their sports within two weeks. They also reported that none of the athletes developed epilepsy at an average follow-up of 3.5 years later. McCrory and Berkovic (2000) followed-up with this research by prospectively investigating videos of acute motor and convulsive manifestations of sport-related concussion. Similarly, they report no abnormalities on neuroimaging or neurological assessments with these athletes. Perron et al. (2001) described the long-term outcomes for patients with concussive convulsions as "*universally good, with no long-term neurologic sequelae and no increased incidence of early or late post-traumatic epilepsy*". However, there is evidence that similar motor response such as the fencing response required greater forces to induce in rats (Hosseini & Lifshitz, 2009), which suggests that there might be increased brain trauma or trauma to deeper structures of the brain (Lighthall, 1988). Unfortunately, similar studies do not exist in humans. Therefore, it is poorly understood if impact seizures associated with concussions are the result of a greater magnitudes of brain trauma and how they differ from other cases of concussions with a loss of consciousness.

Limitations of symptoms duration and neuropsychological performance to determine severity

Previous research describing the link between LOC or impact seizures and severity of injury used measures such as the duration of symptoms and neuropsychological testing. However, such measures reflect a functional impairment rather than severity of structural brain trauma.

The Berlin expert consensus describes persistence of symptoms (greater than 10 to 14 days) as a "*non-specific constellation of symptoms that may be linked to co-existing and cofounding factors that may not reflect an ongoing physiological injury to the brain*" (McCrory, et al., 2017).

For example, the persistence of concussive symptoms have been demonstrated to be influenced by anxiety, coping style, depression, and other psychological factors (McCauley, Boake, Levin, Contant, & Song, 2001; Silver, 2014). Although the duration and intensity of symptoms may describe the severity of a concussion on a clinical stand-point, it is not an accurate reflection of the severity of the structural injury. In a study conducted in a pediatric population, no difference in biomechanical parameters were reported between groups of children with transient concussion when compared to concussion with symptoms lasting longer than four weeks (Post, Hoshizaki, Zemek, & al., 2017). This illustrates that the duration of the symptoms is not a reflection of the severity of the head impacts or the brain tissue deformation.

Neuropsychological tests were designed as tools to help concussion diagnosis and guide return-to-play decisions. They were never designed as a standalone diagnostic tool nor as an indicator for the severity of injury (McCrory, et al., 2017). The results of these tests are influenced by the age, gender, timing of the test, the environment in which they are taken, learning effect, and the symptoms experienced by the subjects (Barr, 2003; Fazio, Lovell, Pardini, & Collins, 2007; Collie, Darby, & Maruff, 2001). Although they might be a useful tool to assist in concussion management, neuropsychological tests are influenced by too many factors to be sensitive enough to determine the severity of the structural injury.

Summary

In summary, the role of LOC as an indicator of severity is ambiguous. Several studies report that LOC may influence the recovery time, but most researchers report that it does not influence neuropsychological performance and cognitive functioning. The studies that particularly investigated the role of LOC often had a limited sample size in the LOC group which could explain the lack of statistical significance on measures such as symptom scores or neuropsychological performance. Furthermore, the results of these measures are influenced by the timing of the tests, anxiety, fatigue and other concussion symptoms (Collie, Darby, & Maruff, 2001). Neuropsychological performance tests may be sensitive enough to distinguish between injury and no-injury (Schatz, Pardini, Lovell, Collins, & Podell, 2006), but they were never designed to distinguish between severity of injury. Therefore, it might be inappropriate to dismiss LOC as an indicator of severity based solely on these measures.

Similarly, the only study reporting an association between impact seizures and severity of injury was conducted on rats (Hosseini & Lifshitz, 2009). This makes it challenging to generalize these results to sports concussions. Researchers who have observed this phenomenon in athletes report no difference in neuropsychological testing or recovery time when compared to athletes with concussions without impact seizures (McCrory, Bladin, & Berkovic, 1997; McCrory & Berkovic, 2000).

The severity of injury as determined by symptom duration or neuropsychological performance does not accurately reflect severity of brain trauma. The discrepancies between the findings of the different studies using these measures represent a challenge when assessing whether LOC and impact seizures represent more severe concussive injuries. Biomechanical measures such as head kinematics and brain tissue deformation would further the understanding of the severity of head impacts associated with these clinical signs of injury.

4. Biomechanics of concussive injuries

The definition of concussion used to be *"The loss of consciousness and associated traumatic amnesia which occurs as the consequences of head trauma in the absence of physical damage to the brain"* (Ward, 1966). As a result, early studies investigating the biomechanics of concussion actually described the biomechanics of cases of concussions with a loss of consciousness. The biomechanical differences between concussions with and without loss of consciousness is therefore poorly understood.

Biomechanics of loss of consciousness

Skull deformation

Gurdjian and coworkers proposed a skull deformation from impact as a mechanism of injury after observing the local and transient skull bending at the impact site of a cadaver after applying a lacquer on the surface of the skull (Gurdjian, Lissner, Hosgson, & Patrick, 1964). They noted stress cracks around the area of impact on the skull suggesting rapid in-bending of the cranial bones. This led to the hypothesis that head impacts result in localized and temporary contact phenomena, where the skull sustains a deformation and quickly returns to its original shape after removal of the load. It was suggested that skull deformation initiates a wave propagation throughout the cranium by creating an area of high pressure underneath the location of the impact that could explain the transient nature of concussions (Gurdjian, Lissner, Webster, Latimer, & Haddad, 1954).

Wave propagation

Walker and his team (1944) were the first to propose pressure wave as the mechanism of brain trauma. They used brain electrical activity to define concussion since LOC was difficult to observe in anesthetized animals. They observed that a spike in intracranial pressure occurred at the same time as a perturbation in electrical activity of the brain following an impact to the head. They suggested that transient pressure waves would alter the neuronal excitation by breaking down the cellular membrane of axons, and that this uncontrolled excitation was responsible for the loss of consciousness.

Other scientists have measured differences in pressure following head impacts. Gurdjian et al. (1954) placed pressure transducers throughout the brain in canines and demonstrated that a peak positive pressure could be observed at the area directly underneath the site of the impact, and an area of negative pressure at the area opposite to the impact site. These areas were named coup and contrecoup pressures (Gurdjian, Lissner, Hosgson, & Patrick, 1964; Gurdjian, Lissner, Webster, Latimer, & Haddad, 1954; Gurdjian, Lissner, Latimer, Haddad, & Webster, 1953). This led to the proposition that concussion were caused by an imbalance of intracranial pressures. This has been hypothesized to create injurious shear stress in the brain tissue and lead to focal injuries (Thomas, Roberts, & Gurdjian, 1967; Gurdjian, Lissner, Latimer, Haddad, & Webster, 1953).

Linear acceleration and pressure gradients

Gurdjian and colleagues demonstrated that linear acceleration correlated well with peak pressures in anesthetized animals (Gurdjian, Lissner, Webster, Latimer, & Haddad, 1954; Gurdjian, Webster, & Lissner, 1955). These researchers proposed that linear acceleration was responsible for the intracranial pressure gradients. Several researchers have demonstrated the focal effects of pure linear acceleration (Thomas, Roberts, & Gurdjian, 1967; Gurdjian, Lissner, Latimer, Haddad, & Webster, 1953; Gennarelli, Thibault, & Ommaya, 1971). Gurdjian et al. (1968) were able to visually monitor the brain motion of Rhesus monkeys by slicing their head in the medial plane and setting a glass plate prior to an occipital impact. They observed that a frontal space was created during the impact and there was movement of the brainstem. He concluded that pressure gradients were formed by skull deformation at the impact site and the subsequent relative motion of the intracranial contents. Pure linear acceleration has been more closely linked to focal injuries such as skull fractures and intracerebral hematomas (Ommaya, Carrao, & Letcher, 1973; Ommaya & Gennarelli, 1974) than concussive injuries.

Rotational acceleration

Holbourn (1943) was the first to suggest that rotational motion was important in creating concussive head injuries. There are two primary theories describing how rotation causes brain injuries (Bradshaw & Morfey, 2001; Hardy, Khalil, & King, 1994; Ommaya & Gennarelli, 1974). The first refers to the inability of the brain to rotate within the skull leading to focal injuries due to shear stress and strains (Bradshaw & Morfey, 2001; Hardy, Khalil, & King, 1994; Gurdjian E. , Hodgson, Thomas, & Patrick, 1968). Many structures create resistance to brain motion within the skull. The anterior fossa is the region with the most focal brain injuries which may be explained by the amount of resistance to motion in the region (Ommaya & Gennarelli, 1974). Since the damage consists mainly of focal injury to the superficial regions of the brain, this theory does not adequately explain a loss of consciousness from concussive impacts.

A second theory proposed that differences in inertial properties of brain tissues led to shearing in zones of changes in density, resulting in both focal and diffuse injuries (Ommaya & Gennarelli, 1974; Gurdjian E. , Hodgson, Thomas, & Patrick, 1968). Holbourn tested the shearing of brain tissue theory as the main mechanism of brain injuries and found that shear stresses and strains were influenced by rotation more than linear translation (Holbourn, 1943). This theory was further developed by Gurdjian et al. (1968) who found that injurious strains in monkeys were created by the difference in mechanical properties of the tissues and the way the forces were transmitted through the different regions (Gurdjian E. , Hodgson, Thomas, & Patrick, 1968).

Diffuse brain injuries comprise diffuse axonal injuries (DAI) and concussions, including LOC (Melvin, Lighthall, & Ueno, 1993). Rotational acceleration has been demonstrated to be a major contributor in the development of diffuse injuries (Ommaya & Gennarelli, 1974; Gennarelli, Thibault, & Ommaya, 1971; Ommaya, Faas, & Yarnell, 1968) suggesting that the most likely mechanism of LOC and concussion is the relative motion between the brain and the skull leading to shearing stresses and strains of the brain tissue.

Gennarelli et al. (1971) undertook biomechanical studies investigating the loss of consciousness associated with head impacts, a phenomenon they termed traumatic unconsciousness. They reported that the rotational component was necessary to induce a loss of consciousness since pure linear acceleration up to 1400 g did not produce LOC in squirrel monkeys (Gennarelli, Thibault, & Ommaya, 1971). It was also noted that LOC could be produced by rotational acceleration in the absence of head impacts but that the magnitude of acceleration needed was double compare to LOC produced by head impacts (Ommaya & Hirsh, 1971b). Rotational acceleration ranging from 5200 to 39 300 rad/s^2 and rotational velocity between 70 and 120 rad/s were reported to induce LOC in monkeys (Ommaya, Carrao, & Letcher, 1973).

Ommaya and Gennarelli (1974) developed the centripetal theory of concussions and proposed that the rotational component of head impacts creates a diffuse effect of strains that progresses in a centripetal manner, with larger strains and tissue deformation on the surface of the brain. They postulated that increased rotational loading would increase the magnitude of the superficial strains and the depth of tissue strains, and that LOC would occur when the magnitudes of strain in the brainstem are sufficient to disrupt the neuronal function. They also claimed that LOC would be accompanied by concomitant and greater damage to the superficial layers of the brain.

Combination of linear and rotational acceleration

As Gennarelli and Ommaya (1971; 1973) demonstrated, rotational acceleration without head impacts only resulted in LOC if the magnitudes of accelerations were extremely high (Ommaya & Hirsh, 1971b). Thus, they postulated that there was a significant contribution from the local effects of impacts on the risk of loss of consciousness. Outside experimental settings, and especially in a sport setting, LOC primarily occurs as a result of head impacts and is likely influenced by both linear and rotational acceleration. Gurdjian (1975) proposed that head injuries could be better explained by a combination of mechanisms: elastic skull deformation, positive and negative pressure, as well as inertial brain lag leading to brain tissue deformation. Interestingly, a study by Bayly et al. (2005) demonstrated that rotational brain movement occurred even in cases of purely linear impacts demonstrating the combined role of these two mechanisms. Due to the complex nature of sporting impacts, it is likely that both linear and rotation acceleration play a role in the risk of LOC or impact seizures. However, the work of Ommaya and Gennarelli demonstrates that a rotational component is key to provoke a loss of consciousness (Ommaya & Hirsh, 1971b; Ommaya & Gennarelli, 1974).

Strain

The hypothesis that rotational acceleration resulted in strain disrupting the function or the integrity of the axons led to the examination of the mechanical effect of strain on white matter axons. At low levels of strain (no structural damage), a neurometabolic cascade is initiated that results in an influx of ions and a release of neurotransmitter resulting in a widespread depolarization of neuronal tissue. Glucose metabolism increases to activate the sodium-potassium pumps and restore homeostasis (Barkhoudarian, Hovda, & Giza, 2011). This pathophysiological model of concussion was established using animal models and there may be some undefined discrepancies between the pathophysiology of animal and human concussions.

Thibault et al. (1990) investigated the recovery of squid axons at different levels of strain. They observed spontaneous recovery of the axon at low levels, and conversely, structural failure at higher levels of strain. Galbraith et al. (1993) measured the electrical dysfunction of a squid axon according to various levels of strain. They reported a transient effect at strains of 0.2 and changes in the morphology of the axon at strains in excess of 0.25. These studies did not assess live tissues and may not represent what happens in live axons. Bain and Meaney (2000) used the optic nerve of guinea pig *in vivo* and measured the disruption of the action potential caused by strain. They reported that strains lower than 0.18 resulted in a reversible injury whereas strain in excess of 0.21 resulted in morphological changes of the neuronal cells of the optic nerve. A range of strains from 0.18 to 0.25 was reported to cause white matter axonal injury. The variation is likely due to the methods used to conduct these experiments as well as the species of the animal tested. Table 1 summarizes the levels of strains and their association with different severities of injury.

Strain levels	**0.05**	**0.10**	**0.15**	**0.20**	**0.25**	
Authors						**Tissue tested**
Thibault et al. (1990)	Spontaneous recovery	Longer axonal recovery	Residual ion deficit	Irreversible injury	Structural failure	Squid axon
Galbraith et al. (1993)	Transient effect of membrane potential			No Axonal recovery	Structural failure	Squid axon
Maxwell et al. (1997)	Transient depolarisation	Localized axonal transport disruption	Loss of axonal transport	Axonal degeneration (bulbs)		Axonal tissue (review)
Bain & Meaney (2000)	Functional disruption			Morphological changes		Optic nerve (Guinea Pig)

Table 1. *Summary of literature on the relationship between levels of strain and axonal dysfunction.*

<u>Paradigm of mechanism of injury for concussion with and without loss of consciousness</u>

Figure 2 is an adaptation of the head injury paradigm mechanism proposed by Ommaya and Gennarelli (1974). The red boxes and arrows describe the mechanism of injury of head impacts producing cerebral concussion and loss of consciousness. In this paradigm, loss of consciousness is caused by the inertial loading from the dynamic impact resulting in rotational acceleration that induces strains diffusely across the brain, interrupting its function. In terms of the severity of loss of consciousness, Ommaya proposes: "*It is logical that the coma of traumatic unconsciousness is either the manifestation of a more severe degree of the same mechanism that produces amnesia* (or other symptoms) *or an uncovering (by a similar or additional mechanism) of an optimally protected part of the brain, or both*". In other words, concussions with loss of consciousness are either caused by greater magnitudes of brain tissue strain or to strain to a specific region of the brain, or both.

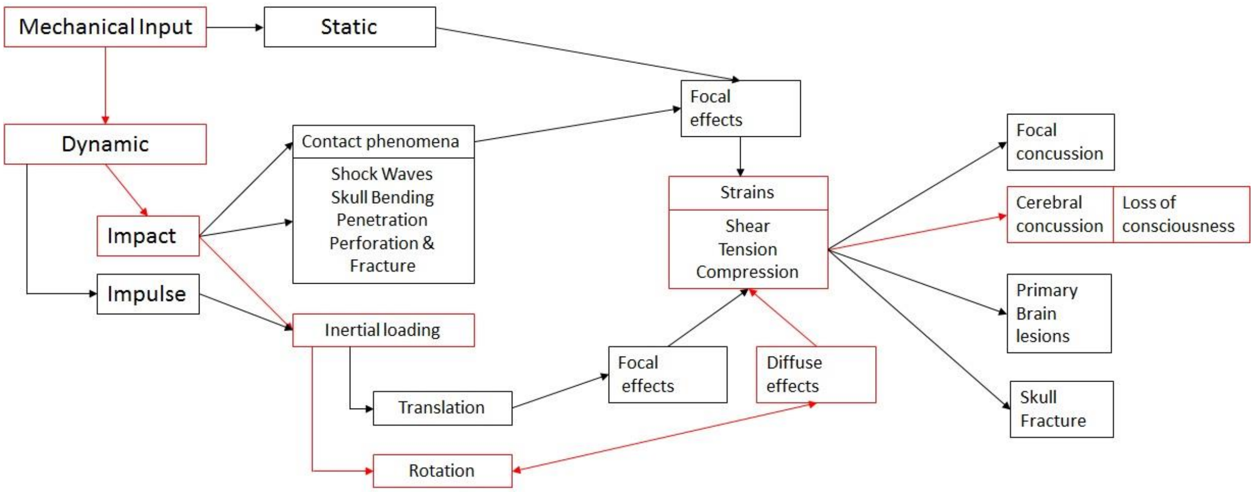

Figure 2. *Paradigm of head injury mechanism proposed by Ommaya and Gennarelli (1974).*

<u>Biomechanics of impact seizure</u>

Only two studies were found to report impact characteristics related to impact seizure responses associated with concussions. McCrory & Berkovic. (2000) suggested a trend towards facial impacts being linked to motor responses but were not able to demonstrate significance. Hosseini & Lifshitz (2009) investigated the prevalence of the fencing response associated with loss of consciousness using online videos obtained on a public domain and then determined the forced needed to induce similar responses in rats. The fencing response was defined as extension and flexion of opposite arms despite body position or gravity. They reported that 66% of their loss of consciousness videos showed a response that could be interpreted as a fencing response regardless of the impact location. A midline fluid percussion was used to induce a brain injury in rats in an attempt to induce a fencing response. A fencing response was observed in 39 of the 44 animals who received a moderate severity impact (1.9 atm) while no animals displayed a motor response following mild impacts (1.1 atm) (Hosseini & Lifshitz, 2009). This suggests that a greater magnitude of impact and brain trauma were necessary to induce an abnormal motor response.

Biomechanics of sports concussions

The biomechanics of concussions as defined by a loss of consciousness was predominantly conducted on animal and cadaveric models of head impacts. The results obtained from these models are not easily comparable to human concussions in sports. The definition of the injury and the field of concussion biomechanics research have evolved greatly since these studies were published. The diagnosis of a concussion is no longer based on loss of consciousness but on the presence of a variety of symptoms such as headache, nausea, dizziness, etc. following a head impact (McCrory, et al., 2017). Researchers have started using anthropometric dummies to describe head kinematics associated with head impacts (See Chapter 4) and better understand the association between peak linear and rotational acceleration and risk of concussion in sports. This section will describe the biomechanics associated with head impacts in football and boxing.

Viano and colleagues (2007) reconstructed 25 helmet-to-helmet collisions and falls in American football. They reported average peak linear and rotational accelerations of 94 g and 6432 rad/s^2 for concussive impacts and 67.9g and 5209 rad/s^2 for non-concussive impacts. One of the main limitation of this study was the method used to calculate impact velocity. They used the length of the helmet to calibrate their distance which resulted in the average velocity for concussive impacts to be approximatively 9.3 m/s. This method of measuring velocity is not validated and may results in an overestimation. Another major limitation was their test setup for collisions. It consisted of components of a Hybrid III headform and neck suspended by wires of total weight of 15.1 kg being dropped on another Hybrid III headform, neck and torso. The drop was guided which did not allow for the reproduction of glancing impacts sometimes observed in American football and resulted in more energy being directed through the center of gravity of the head. In addition, they only included the most obvious cases of concussions which may have resulted in an overestimation of the peak linear and rotational acceleration associated with concussive impacts. Zhang et al. (2004) used similar data to establish a threshold for injury in terms of linear and rotational acceleration. The values suggested for a 50% likelihood of concussion are 82 g and 5900 rad/s^2 for peak linear and rotational acceleration, respectively. These thresholds do not take into account the event that led to the injury (falls vs collisions).

Kendall (2016) demonstrated that peak linear and rotational acceleration were influenced by the type of impact event and therefore should be analyzed separately. This phenomenon can be observed in boxing where different types of punches results in different magnitude of peak accelerations. Stojsih (2008) reports peak linear acceleration for hooks, jabs, and crosses in male amateur boxers of 62, 41, and 45 g respectively. The peak rotational acceleration were 6440, 4927, and 4779 rad/s^2 for hooks, jabs, and crosses, respectively. These values were influenced by the impact velocity, the technique, and the striking mass (male vs female). Fife and colleagues (2013) measured the linear acceleration of the head in Olympic boxers using a Hybrid II headform. They reported an average of 71.2 g for hooks, 51.5 g for a punch to the jaw, 17.11 g for uppercuts, and 52.26 g for punches to the forehead. Viano et al. (2005b) used 11 Olympic boxers to impact the Hybrid III headform and compared the peak linear and rotational acceleration to American football head impacts. The values of linear acceleration reported for punches to the forehead, hooks, punches to the jaw and uppercuts were similar to those reported by Fife (2013). However, Viano and colleagues' magnitudes of rotational acceleration were greater than those reported by Stojsih (2010), particularly for the hooks. The values of peak linear and rotational acceleration associated with head impacts in American football and boxing are summarized in Table 2.

Authors	**Sport**	**Type of impact event**	**Peak linear acceleration (g)**	**Peak rotational acceleration (rad/s^2)**	**Measure of Injury**
Viano et al. (2007)	American football	Helmet-to-helmet and falls	94	6432	Average concussive impacts
Zhang et al. (2004)	American football	Helmet-to-helmet and falls	82	5900	50% risk of concussion
Stojsih (2018)	Amateur boxing	Hook	62	6440	Average values for impacts
		Jab	41	4927	
		Cross	45	4779	
Fife (2013)	Olympic Boxing	Hook	71.2	-	Average values for impacts
		Jaw punch	51.5	-	
		Uppercut	17.1	-	
		Forehead punch	52.3	-	
Viano et al. (2005b)	Olympic boxing	Hook	71.2	9306	Average values for impacts
		Jaw punch	48.8	6896	
		Uppercut	24.1	3181	
		Forehead punch	47.8	5452	

Table 2. *Peak linear and rotational acceleration associated with boxing and football head impacts.*

<u>Summary</u>

Early biomechanical research on head injuries conducted on animals and cadaveric models provide information on the mechanism of injury related to concussion with and without loss of consciousness. It is understood that the combination of linear and rotational acceleration results in strain in the brain tissue that leads to alteration in neuronal function. Another important concept obtained from these studies was the importance of rotational acceleration in the provocation of loss of consciousness. Peak linear and rotational acceleration are now commonly measured in more recent biomechanical research and are used to distinguish between injury and no-injury impacts in American football and to characterize the relative risk of injury associated with different events in boxing. Although extensive studies have been done using these metrics, none have compared the magnitudes of acceleration between concussion with and without LOC and impact seizures. However, examining peak acceleration may not fully describe the mechanics responsible for loss of consciousness in sports. Since head accelerations cause strains in the brain tissue that is responsible for the concussive injury, measuring strain-based metrics using finite element modeling is appropriate to describe the severity of injury associated with concussions with and without loss of consciousness or impact seizures. Describing the level of strain associated with loss of consciousness and impact seizures in sport-related head impacts will further the understanding of the severity of injury associated with these signs as strain relates to the structural trauma.

5. Head and brain injury surrogate models

The biomechanics of brain injury have been investigated using animals, cadavers, anthropometric test devices (ATD), and finite element models (Gurdjian, Hodgson, & Patrick, 1968; Gennarelli, Thibault, & Ommaya, 1971; Viano, Casson, Pellman, King, & Yang, 2005; Kleiven, 2007). Each of these methods have limitations. Although animals provide the opportunity for real-time assessment of the physiological effects of the injury, the applicability of the results to human injuries is hard to determine due to unknown scaling factors. Cadavers are advantageous because of the same weight distribution and geometry of the head as humans, but tissue decomposition or effects of embalming may produce inconsistent responses (van Dommelen & Peters, 2009). Furthermore, cadaveric models may not appropriately represent what happens in a live head. ATDs were created to study brain injury and provide consistent and replicable responses while mimicking the geometry and mass distribution of the human head. They were developed to approximate the complex human response with a simplified model (Patrick, 1973)

Anthropometric test devices

Injury reconstructions using ATDs are useful to understand head impact biomechanics. Their advantages are their durability and their shared characteristics with real human heads such as mass, geometry, and skin characteristics. Some features of the human head have to be sacrificed in ATDs to allow for repeatability. However, there are large individual differences in responses between humans and since ATDs falls within the range of possibilities, they can be a valuable tool to understand the mechanics of injury of a given population (Patrick, 1973). These headforms are equipped with sensors that measures biomechanical variables linked to brain injury such as linear and rotational acceleration (Viano, King, Melvin, & Weber, 1989).

There are many types of headforms available for impact testing. One of the most commonly used headform is the Hybrid III headform. The Hybrid III headform has been validated using peak linear acceleration from cadaveric head impacts to the frontal area (Mertz, Biofidelity of the Hybrid III head, 1985). It was originally created to be used in car crash scenarios and evaluate passenger safety, and is considered the standard in the automobile safety industry (Mertz, Prasad, & Irwin, 1997; Prasad, 2015). In a study that compared the responses of several headforms, including the Hodgson-WSU headform, the Hybrid III headform was determined to produce the closest response to cadaveric data (Mertz, 1985). The physical dimensions of the Hybrid III headform can be found in Table 3.

Physical characteristics	**Hybrid III headform**
Mass (kg)	4.54
Circumference (m)	0.58

Table 3. *Physical characteristics of the Hybrid III headform.*

The Hybrid III headform can be attached to a neckform which has been known to have an important influence on the peak accelerations of the headforms. The Hybrid III neckform is the most commonly used in impact reconstructions but is limited by its asymmetry and may induce a bias in the sagittal plane (Deng, 1989). This design may be appropriate in car-crash scenarios, but sports concussions can occur from various locations and directions of impact. In order to better understand the effects of these impacts, an unbiased neckform that is built with the same specifications as the Hybrid III neckform but without the built-in directionality could eliminate this bias and result in more appropriate head acceleration responses. A neckform with the same mass and geometry as the Hybrid III neckform was designed at the University of Ottawa (Ottawa, Canada). The anterior slits and continuous posterior rubber of the Hybrid III neckform were replaced with uniform circular steel and rubber plates held together by a cable tightened with a bolt similarly to the Hybrid III manufacturer's specifications. A study performed by Walsh et al. (2018) demonstrated that for events of duration 5-10 milliseconds there were no significant differences in peak linear and rotational acceleration between the Hybrid III and unbiased neckforms. The unbiased neckform was used in this thesis since it was engineered to be free of bias in all directions under any impact conditions. A comparison of the physical characteristics between the Hybrid III and unbiased neckforms can be found in Table 4.

Physical characteristics	**Hybrid III neckform**	**Unbiased neck**
Mass (kg)	1.54	1.30
Height (m)	0.12	0.13
Diameter (m)	0.08	0.08
Cable torque (Nm)	1.40	1.40

Table 4. *Comparison of the physical characteristics of the Hybrid III and unbiased neckforms.*

Finite element modeling

Kendall (2016) reported that the shape of the linear and rotational acceleration curves, including the peak values of acceleration, are influenced by the type of head impact event. LOC is observed in several different events including punches, falls, and collisions, all exhibiting different curve shapes and peak acceleration values (Kendall, 2016). Therefore, the peak values of linear and rotational acceleration do not accurately predict LOC. The signs and symptoms of a concussion, including LOC, are proposed to be the results of the neurometabolic cascade caused by mechanical deformation of the neuron (Giza & Hovda, 2001). The cascade includes a mass depolarization of neurons followed by a depressive state that causes impairments of certain functions of the brain (Giza & Hovda, 2001). The brain tissue deformations resulting from the motion of the brain may be a more appropriate metric. Strain has been demonstrated to induce physiological response in the neurons consistent with concussive injuries (Galbraith, Thibault, & Matteson, 1993; Geddes, Cargill, & LaPlaca, 2003). Laboratory reconstructions and finite element modeling allow for the estimation of strain-based metrics such as maximum principal strain, cumulative strain damage measure, and strain rate.

Finite element modeling is a numerical modeling method that characterizes how mechanical loading affects a system. These models take into account the external forces, the geometry of the brain and its material properties and provide an approximation of the strain the brain has experienced (Fish & Belytschko, 2007). This approach is advantageous because it can provide an understanding of the mechanisms of injury without injuring animals or humans and is reproducible.

Wayne State University Brain Injury Model (WSUBIM)

In this thesis, the Wayne State University Brain Injury Model (WSUBIM) was used because of the better stability of the brainstem and cerebellum when compared to other finite element models. Although the motion or pressure of the brainstem and cerebellum are not validated in any finite element brain models, the WSUBIM responses in these regions have a better face validity, i.e. the response increases as the severity of loading condition increases (inbound velocity and resulting accelerations). The calculated values of strain for these regions also remain within reasonable ranges. In addition, the WSUBIM has more elements and is more refined which makes it more appropriate when investigating specific brain regions.

Material Properties

The Wayne State University Brain Injury Model (WSUBIM) developed by Zhang et al. (2001) will be used to obtain the maximum principal strain, the cumulative strain damage measure at 10 %, and strain rate in the brain regions of interest for punches representations in boxing and American football reconstructions. The three-dimensional loading curves obtained from the reconstructions will be applied to the WSUBIM with the same method described by Zhang et al (2004). The simulations will be run using PAM-CRASH (ESI, Farmington Hills, MI, USA). The WSUBIM includes the skull, scalp, dura mater, pia mater, falx cerebri, falx and tentorium cerebelli, cerebrospinal fluid, lateral and third ventricles, cerebrum (grey and white matter), cerebellum, brainstem, parasagittal bridging veins, and venous sinuses for a total of 314, 500 elements (hexahedral brick and shell) and a mass of 4.5 kg (Zhang, et al., 2001). The brain and head material properties are shown in Tables 5 and 6. The brain tissue was modelled using a combination of a linear viscoelastic model and a large-deformation theory (Zhang, et al., 2001) . The shear modulus of the viscoelastic brain was characterized as:

$G(t)=G_\infty +(G_0 - G_\infty)e^{-\beta t}$

Where G_0 is the short term shear modulus, G_∞ is the long term shear modulus and β is the decay factor (Zhang, et al., 2001) . The cerebrospinal fluid layer was modelled as solid elements with a low shear modulus and was applied with a sliding but no separation condition to represent the brain skull interaction (Zhang, et al., 2001).

Brain region	**Density *p* (kg/mm^3)**	**Bulk modulus *K* (GPa)**	**Short-term shear modulus G_0 (Pa)**	**Long-term shear modulus G_∞ (Pa)**	**Decay constant (s^{-1})**
Grey matter	1.04E-06	2.19	4.10E+04	7.80E+03	4.00E+02
White Matter	1.04E-06	2.19	3.40E+04	6.40E+03	4.00E+02
Brainstem and cerebellum	1.04E-06	2.19	5.80E+04	7.80E+03	4.00E+02

Table 5. *WSUBIM material properties of the brain*

Anatomical feature	**Density (ton/m3)**	**Bulk modulus (GPa)**	**Shear modulus (GPa)**	**Poisson's ratio**
Scalp	1.2	E=1.67e-2		0.42
Skull	2.1	4.76	3.279	0.22
Cerebrospinal fluid	1.04	2.19E-01	5.00E-05	
Dura, falx and tentorium	1.1333	E=3.15e-2		0.45
Pia	1.133	E+1.15e-2		0.45
Bridging veins	1.133	EA=1.9N		0.45
Facial bone	3	E=5.54		0.22

Table 6. *WSUBIM material properties of the head*

Model Validation

The WSUBIM was validated for intracranial pressure responses against unembalmed cadaveric head impacts from Nahum et al. (1977), in which intracranial pressure was measured with pressure transducers at five different locations to obtain the changes in intracranial pressure during the impact. The WSUBIM was validated for intracranial and ventricular pressure responses with Troseille et al.'s (1992) series of re-pressurized cadaveric impact tests. The authors used a 12-accelerometer array to obtain the 3D kinematics of the head and pressure transducers in the subarachnoid space and the ventricular system. Finally, Zhang et al. (2001) validated the WSUBIM against brain motion data obtained from a high-speed biplanar x-ray system combined with the use of radio-opaque neutral density targets measuring the relative motion between the skull and the brain (Hardy, et al., 2001). The WSUBIM was used to analyze brain injuries, including sport concussions and the responses were consistent with the literature associated with cadaveric impacts and anatomical testing of tissue (Zhang, Yang, & King, 2004; Viano, Casson, Pellman, King, & Yang, 2005).

Brain tissue deformation metrics

Maximum principal strain

Maximum principal strain obtained using finite element modeling is a useful variable to relate physical reconstructions to the level of strains leading to mechanical failure described from anatomical testing. Studies using physical reconstructions and FE modeling to study concussions in sports have reported MPS as a useful variable to predict the risk of concussive injury (Patton, McIntosh, & Kleiven, 2013; Patton, Mc Intosh, & Kleiven, 2015; Kleiven, 2007; Viano, Casson, Pellman, King, & Yang, 2005). Patton et al. (2013) demonstrated that MPS in the thalamus, white matter, and corpus callosum were the most predictive of concussions in Australian rules football, rugby league, and rugby union unhelmeted impacts. On the other hand, Kleiven (2007) reported that MPS in all brain regions with the exception of the brainstem had the ability to distinguish between cases of concussion and no injury impacts in American football, with the best predictions using MPS were found in the grey matter and the corpus callosum. Viano et al. (2005) obtained similar results using a different FE model on a subset of Kleiven et al. (2007)'s cases stating that MPS associated with concussive cases was significantly greater than MPS in non-injurious impacts.

Cumulative strain damage measure

Cumulative strain damage measure (CSDM) represents the volume of the brain that experienced a pre-set level of strain (Bandak & Eppinger, 1994). Patton et al. (2015) analyzed multiple FE modeling output variables associated with brain injury and reported that CSDM at 5% in the thalamus had the best association with concussions. The authors also demonstrated significant association between CSDM at 5, 10, and 15% in all part of the brain and concussions with the exception of the brainstem at 10 and 15%. CSDM at 10% was also reported to be able to distinguish between impacts leading to concussions and impacts not leading to concussions in American football in all brain regions with the exception of the brainstem and midbrain (Kleiven, 2007).

Strain Rate

King (2003) suggested strain rate as a predictor of brain injury due to the viscoelastic properties of the brain. Strain rate is the only metric cited in the literature to be associated with a loss of consciousness from physical reconstructions of sports-related concussions (Viano, Casson, Pellman, King, & Yang, 2005). Viano et al. (2005) reported that strain rate in the midbrain correlated well with LOC in American football impacts. However, their sample only included four cases of LOC limiting the conclusions that could be made. Galbraith et al. (1993) reported the physiological response of the neurons to strain was dependent upon the rate of loading, stating that the magnitude of the depolarization and time needed to recover increased as the strain rate increased. Using physical reconstructions and FE modeling, Patton et al. (2015) reported that strain rate in the thalamus and corpus callosum was highly associated with concussions demonstrating that this metric could be useful in predicting clinical outcomes.

Overall, MPS, CSDM at 10% and strain rate have been shown in the literature to be good variables to measure the risk of concussive injuries in sports and may be useful in predicting the mechanisms of injury associated with a loss of consciousness.

Table 7 displays a summary of the values of MPS, CSDM at 10%, and strain rate associated with sports-related concussions in different part of the brain.

Authors	Model	Sport	Injury Measure	Brain tissue deformation metric	Brain region	Value
Zhang et al. (2003)	WSUBIM	American football	50% risk of concussion	Strain rate	Midbrain	60.0 s^{-1}
Zhang et al. (2004)	WSUBIM	American football	50% risk of concussion	Strain	Midbrain	0.19
Viano et al. (2005)	WSUBIM	American football	Mean for concussive injuries	Strain	Midbrain	0.34
					Thalamus	0.38
				Strain rate	Midbrain	79.3 s^{-1}
					Thalamus	74.4 s^{-1}
Kleiven (2007)	KTH	American football	50% risk of concussion	Strain	Corpus callosum	0.21
					Gray matter	0.26
				Strain rate	Gray matter	48.5 s^{-1}
				CSDM10	White matter	0.47
Kimpara et al. (2012)	THUMS (modified)	American football	50% risk of concussion	Strain	Not specified	0.31
				CSDM10	Not specified	0.18
McAllister et al. (2012)	Dartmouth SSM	American football and ice hockey	Mean for concussive injuries	Strain	Corpus callosum	0.28
				Strain rate	Corpus callosum	54.0 s^{-1}
Patton et al. (2013)	KTH	Rugby and Australian rules football	50% risk of concussion	Strain	Midbrain	0.15
					Corpus callosum	0.15
					Gray Matter	0.27
Patton et al. (2015)	KTH	Rugby and Australian rules football	50% risk of concussion	Strain	Thalamus	0.13
					Corpus callosum	0.15
					White matter	0.26
				Strain rate	Thalamus	24.0 s^{-1}
					Corpus callosum	25.1 s^{-1}
					Midbrain	30.9 s^{-1}
					Gray Matter	57.4 s^{-1}
				CSDM10	Midbrain	0.36

Table 7. *Brain tissue deformation (MPS, CSDM10, strain rate) associated with concussive head impacts in sports.*

Limitations of finite element models

Finite element models are created as representations of the geometry and anatomy of the human head as well as the mechanical properties of the structures of the brain. This allows for the interpretation of how brain motion following a head impact affects the magnitude and location of brain tissue trauma. Many assumptions are made in the creation of models such as their geometry, material constitutive laws and material properties, which leads to differences between models. Modellers use different properties when simulating the skull-brain junction, the skull thickness, and the properties of the brain matter, all influencing the brain's response to injuries. The brain material properties chosen for finite element models are based on animal or cadaveric data and may differ between studies depending on the testing methods used to prepare the specimen or conduct the experiment. The material properties chosen for brain region such as the thalamus or corpus callosum are not specific to these particular regions. These regions are represented in FE models (including the WSUBIM) by a volume of elements with the material properties of grey matter for the thalamus and white matter for the corpus callosum. The assumptions made by the creators of these models result in each finite element model of the brain being different from each other. Also, due to the limited validation data available, it is impossible to know which model is more accurate. There are several recent modellers who have attempted to improve the level of sophistication of FE brain models by adding white matter tracts or changing the properties of the brain. However, without the ability to confirm the responses obtained from these models, it is impossible to determine whether these changes improved accuracy. Most FE models were validated using the same set of data for pressure (Troseille, Tarriere, Lavaste, Guillon, & Domont, 1992) and brain motion (Hardy, et al., 2001). The number of elements, the material properties and boundary conditions chosen by the modellers, the level of anatomical accuracy and details can change the absolute values obtained via different FE models but is unlikely to change the relationship between distinct datasets since they shared the same validation. Therefore, FE models can be a useful tool to make comparisons between populations with different clinical outcomes.

Summary

ATDs and finite element models can play a useful role in understanding the mechanics of brain injuries. The durability and the reliability of the Hybrid III headform makes it an important tool to study the biomechanics of head impacts in sports. The Hybrid III headform is used to capture linear and rotational acceleration which may play a role in the risk of loss of consciousness in sports. The acceleration-time curves are used as input for the WSUBIM to compute brain tissue deformation metrics such as the maximum principal strain, cumulative strain damage measure, and strain rate. These metrics provide information regarding the severity of head impacts associated with loss of consciousness and impact seizures in sports-related concussions. Research has demonstrated that finite element models were sensitive enough to distinguish between cases of injury and no-injury head impacts in several brain regions.

6. Brain regions associated with loss of consciousness and impact seizures

Regions of the brain associated with loss of consciousness

In a normal functioning brain, consciousness is maintained through the activity of four principal structures. The reticular formation, more specifically the afferent reticular activating system (ARAS), located in the brainstem sends a signal to the reticular nuclei of the thalamus through the reticulo-thalamic tracts. The thalamus then redirects the signal to the cerebral cortex via white matter tracts (cortico-thalamic projections) (Daube, 1986; Paus, 2000; Gosseries, et al., 2011). Previous studies have demonstrated that lesions to each of these structures can be linked to loss of consciousness. In traumatic brain injuries, lesions to the cerebral cortex, the thalamus, the white matter, and the brainstem have been shown to produce LOC and that the depth and the duration of LOC is correlated to the depth of the lesions (Gentry, Godersky, & Thompson, 1988; Levin, et al., 1988; Levin, et al., 1997).

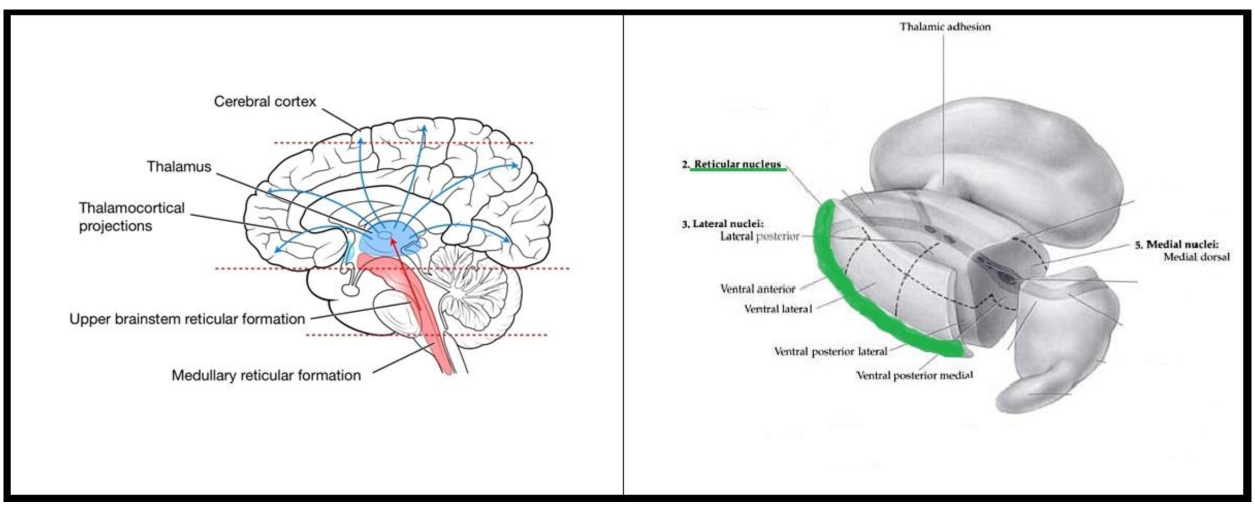

Figure 3. *Anatomy of consciousness [left figure modified from (Benerroch, Daube, Flemming, & Westmoreland, 2008); right figure modified from (Neurosurgery, 2017)].*

Brainstem

The brainstem has been linked to consciousness since the early 1930s based on work done by Bremer (Bremer, 1935a; Bremer, 1935b; Bremer, 1936; Bremer, 1938b). He reported the activation of the cortex, and therefore consciousness, was dependent on the afferent sensory impulses relayed from subcortical structures. He demonstrated that bilateral lesions of the brainstem led to a cerebral electrical activity level consistent with deep sleep (Bremer, 1935a; Bremer, 1935b; Bremer, 1936).

Arousal properties of the brainstem reticular formation were described in a series of experiments demonstrating that electrical stimulation of the rostral portion of the reticular formation of dormant animals produced cortical activation measured by an EEG similar to that of the normal arousal state as well as behavioral signs of wakefulness (Segundo, Arana-Iniquez, & JD, 1955; Moruzzi & Magoun, 1949; French, Von Amerongen, & HW, 1952; French, Verzeano, & Magoun, 1953a; French, Verzeano, & Magoun, 1953b). These results completed Bremer's work by explaining how afferent impulses influenced the diffuse arousal of the brain. This portion of the reticular formation was labeled the afferent reticular activating system (ARAS) (Moruzzi & Magoun, 1949; French, Von Amerongen, & Magoun, 1952; French, Verzeano, & Magoun, 1953a; French, Verzeano, & Magoun, 1953b). Experiments involving cats and monkeys demonstrated that destruction of the central reticular core of the brainstem produced chronic unresponsiveness (Lindsey, Bowden, & Magoun, 1949; Lindsey, Schreiner, Knowles, & Magoun, 1950) which led to the conclusion that maintenance of consciousness was decisively dependent upon the integrity of the ARAS. The reticular formation also has descending functions. The caudal portion of the reticular formation (especially the ventro-medial segment of the medulla) has been found to play an inhibitory role on muscle tone and reflex activity, while the rostral parts (the pontomesencephalic tegmentum) produce an activating effect on motor activities (Magoun & Rhines, 1946; Rhines & Magoun, 1946). These results led to the suggestion that LOC was caused by a functional disruption of the ARAS of the brainstem, disabling its stimulation to the thalamus (Shaw, 2002). Consequently, the inhibitory responses of the medial portion of the thalamus would not be overridden and the result would be a loss of consciousness (Shaw, 2002). Reactivation of the cortex is regained once the reticular formation has recovered and can override the inhibitory response from the medial thalamus (Shaw, 2002).

In support of loss of consciousness being the result of the inactivation of the ARAS following a head impact, Foltz et al. (1953) demonstrated that electrical activity was significantly more depressed in the reticular formation than in the cerebral cortex. The authors debated whether the depression in the reticular formation was caused by the head impact or from the decrease in afferent stimulating activity from the adjacent lemniscal pathways. They recorded measured sensory evoked potentials (SEPs) in both the reticular formation and the lemniscal pathways and reported that, following head injury, the short latency lemniscal pathway was not affected but the longer latency reticular SEP was lost or significantly decreased in amplitude with LOC (Foltz, Schmidt, & Ward, 1953). These results suggest that the decreased activity in the reticular formation was in fact caused by the head impact. These results illustrate the recordings of only one of the eight animals tested and the recordings were not started until at least 20 minutes after the impact. Considering that loss of consciousness usually presents with immediate and sudden onset and is short-lived, it may not represent the initial response following the head impact. Ommaya et al. (1973) were able to record EEG and SEPs as soon as one minute following the head impact and showed that EEG recordings were minimally altered following head impacts but that SEPs displayed significant changes and correlated strongly with the period of unconsciousness in chimpanzees. Ommaya's results differed from Foltz's as both short latency lemniscal and long latency reticular pathways were equally affected by the head impact. The results were later reproduced in squirrel monkeys for which cortical SEPs corresponding to brainstem function were abolished immediately following the head impact and remained absent throughout the duration of unconsciousness (Ommaya & Gennarelli, 1974), leading the authors to the conclusion that loss of consciousness induced by head impacts was the result of a disruption of the ARAS.

Alterations in neuronal structure, axonal degeneration, as well as cytological and morphological changes have been observed in the general brainstem region, specifically in the reticular substance following experimental head impact with a loss of consciousness (Plum & Posner, 1980). Chromatolysis in the brainstem, which indicates the disintegration of the chromophil substance and is an indicator of traumatic damage to neurons, was also noted 15 minutes post-impact and was more prominent in the reticular formation than the rest of the brainstem, (Windle, Groat, & Fox, 1944).

Groat & Simmons (1950) and Frieded (1961) observed evidence of brainstem neuron loss following head impact with loss of consciousness in guinea pigs thirteen months post-concussion and after eight days in cats (Groat & Simmons, 1950; Friede, 1961). Marked but reversible changes in mitochondria and edema have also been seen in the medulla of rats (Bakay, Lee, Lee, & Peng, 1977). In addition, Oppenheimer (1968) suggested that neurons in the brainstem exhibited some form of degeneration after a head impact with loss of consciousness (Oppenheimer, 1968). Jane (1985) reported that this degeneration was mostly in the neurons of the brainstem and absent from cells located in the cerebral white matter (Jane, Steward, & Gennarelli, 1985). Similarly to Foltz et al. (1953), such response to head impact takes place after a lengthy period of time, in this case hours to months after the initial impact, suggesting that the neurons of the brainstem are susceptible to delayed-onset neurodegeneration and possibly explaining the link between LOC and long-term disability.

Cerebral cortex

Disruption of the cerebral cortex as an explanation for impact-induced LOC was first suggested by Walker and his team (1944) when they formulated the convulsive theory of loss of consciousness. Symptoms associated with head impacts with a loss of consciousness were suggested to be similar to symptoms of generalized epileptic seizures (Symonds, 1935; Symonds, 1974; Plum & Posner, 1980). According to advocates of the convulsive theory, both conditions are characterized by immediate loss of consciousness typically lasting only a few minutes and resemblances between symptoms of concussions and in epileptic patients in between seizures, such as irritability, depression, insomnia, anxiety, and fatigue (Shaw, 2002). It was suggested that convulsive symptoms were missed in human subjects or misinterpreted by bystanders, resulting in scientists ignoring this phenomenon in their research (Shaw, 2002). Another possibility is that the phenomenon described as a convulsion was in fact impact seizures.

Duret (1920) suggested that concussions had an initial neuronal excitatory period rather than a depressive one, therefore proposing that concussions be separated into two periods: an initial convulsive period and a longer quiescent period. The initial convulsive presentation was often reported in animal experiments but overlooked by many, in order to focus on the quiescent phase (Walker, Kollros, & Case, 1944). Walker et al. (1944) observed an epileptic-like wave on EEG recordings following concussion. They concluded that brain deformations in the cerebral cortex from head impacts led to diffuse neuronal depolarization resulting in hyperexcitability followed by a longer paralytic period represented by depressed cortical rhythms (Walker, Kollros, & Case, 1944). The over-excitation of the cerebral cortex would prevent its activation by the brainstem ARAS, resulting in a loss of consciousness (Shaw, 2002).

EEG studies have described an initial spike in cortical activity following a concussive blow (Walker, Kollros, & Case, 1944). Glucose hypermetabolism, increased oxygen metabolic rate, and increased cerebral blood flow measures observed following LOC-inducing head impacts in animals are consistent with seizure-like activity (Nilsson & Nordstrom, 1977a; Meyer, Kondo, Nomura, Sakamoto, & Teraura, 1970; Yoshino, Hovda, Kawamata, Katayama, & Becker, 1991; De Witt, et al., 1986).

Ionic shifts and neurotransmitter release suggestive of increased activity are a well-documented phenomenon following concussions supporting the concept that head impacts can result in an abnormal depolarization pattern. There is evidence of extra-cellular potassium in the hippocampus of rats following concussive injuries (Katayama, Becker, Tamura, & Hovda, 1990). There is also evidence for the presence of extra-cellular excitatory amino-acids such as glutamate and aspartate following head impacts (Palmer, Marion, Botscheller, Swedlow, & Styren, 1993; Dixon, Clifton, Lighthall, Yaghmai, & Hayes, 1991; Faden, Demediuk, Panter, & Vink, 1989). While numerous scientists were able to demonstrate this, the relationship between concussions, cerebral excitation, and release of excitatory amino acids was best demonstrated by Nilsson et al. (1994). Their team demonstrated a substantial release of excitatory amino acids following head trauma that coincided with seizure-like activity in rats. This high release of excitatory amino-acids can also be observed in clinical seizures (Ronne-Engstrom, et al., 1992).

Thalamus

The thalamus is a relay station between cortical and subcortical regions of the brain. It is involved in the process of consciousness in both stimulating and inhibiting manners. The central thalamic neurons have strong connections with both the ascending projections of the brainstem arousal system and descending projections from the cortical systems responsible for the level of arousal associated with variations in cognitive efforts (Van der Werf, 2002; Schiff, 2008). Electrical stimulation of the medial thalamus has been shown to elicit sleep-like responses in animals suggesting that the medial nuclei of the thalamus act as a pacemaker that regulates the level of consciousness with input from the brainstem reticular formation (Dempsey & Morison, 1942; Morison & Dempsey, 1943). Autopsies of both non-traumatic and traumatic injuries resulting in vegetative states have demonstrated widespread neuronal death in the thalamus (Adams, Graham, & Jennett, 2000). Bilateral focal injuries to central thalamic nuclei are shown to produce global disorders of consciousness (Castaigne, et al., 1981; Schiff & Plum, 2000).

White Matter

White matter tracts connect regions of the brain. A disruption of their signaling could result in the interruption of a function that necessitates multiple regions to work, including the maintenance of consciousness. A number of scientists have reported evidence of white matter injury leading to loss of consciousness. Studies on traumatic brain injuries demonstrated that isolated lesions to the white matter, such as diffuse axonal injuries, could lead to prolonged loss of consciousness (Gentry, Godersky, & Thompson, 1988; Adams, Graham, Murray, & Scoot, 1982). There is also evidence of white matter injury in cases of LOC using diffuse tensor imaging (DTI). DTIs are used to assess alterations at the microstructural levels, usually in the white matter in the case of head injuries (Le Bihan, et al., 2001). An increase in mean diffusivity (MD) is an indicator of axonal swelling, a decrease in fractional anisotropy is a marker of microstructural changes, and an increase in radial diffusivity signifies a de- or dys-myelination of the neurons (Le Bihan, et al., 2001). Wilde and colleagues (2016) showed that mild traumatic brain injuries with loss of consciousness showed an increased MD in the uncinate fasciculi (UF) and inferior frontal occipital fasciculi (IFOF) bilaterally when compared to a control group that sustained orthopedic injuries. They also showed that the MD in the UF was higher in a subgroup with mTBI and LOC when compared to a no-LOC mTBI group (Wilde, et al., 2016). In contrast, the mild traumatic injury group that did not lose consciousness did not differ in MD for any of the tracts analyzed from the orthopedic group. Two studies investigating the difference between DTI measures on veterans following blast-related concussions demonstrated that subjects who had lost consciousness displayed differences in white matter indices (FA and RD) in several brain regions, including the corpus callosum, when compared to subjects who only had alterations of consciousness (Matthews, Spadoni, Lohr, Strigo, & Simmond, 2012; Sorg, et al., 2014).

Corpus callosum

The corpus callosum is the largest white matter structure of the human brain (Hofer & Frahm, 2006). The orientation of its fibers makes it particularly susceptible to injury from lateral impacts, which are the most common impact direction linked to concussions in sports (Pellman, Viano, Tucker, & Casson, 2003; Mc Intosh, Mc Crory, & Comerford, 2001). Gennarelli et al. (1982) demonstrated that diffuse axonal injury in the corpus callosum from lateral impacts was associated with traumatic coma of longer duration. Gentry et al. (1988) showed that injury to the corpus callosum was associated with greater alteration in consciousness as measure by the GSC. However, lesions to the corpus callosum are often associated with lesions of the brainstem which may play an influential role in a loss of consciousness (Adams, Graham, Murray, & Scoot, 1982; Gennarelli, et al., 1982; Gentry, Thompson, & Godersky, 1988).

Regions of the brain associated with impact seizures

Hosseini & Liftshitz (2009) postulated that the fencing response would involve a similar neural circuit as the asymmetrical tonic neck reflex in human infants: the lateral vestibular nuclei of the brainstem (Xiong & Matsushita, 2001). As such, they measured the neuronal nuclear volume in this region and reported that the mean nuclear volume loss in these neurons 10-15 minutes post injury was significantly greater in the moderate severity impact group than the mild impact group or a sham control group. However, they did not investigate other brain regions nor did they make the distinction between animals with and without the fencing response. Others have postulated that this type of response is analogous to convulsive syncope (McCrory & Berkovic, 1998) which are suggested to be the result of a loss of cortical inhibition in conjunction with a brainstem reflex activation (Gastaut & Fisher-Williams, 1957; Duvoisin, 1962).

Impact seizures

For the purpose of this thesis, the abnormal motor responses studied will consist of cases of impact seizures defined as a maintained tonic (few seconds) bilateral, unilateral, or asymmetrical flexion and/or extension posture of the upper limbs. It is acknowledged that these postures are typically associated with similar responses in the lower extremities but only cases with upper body posturing will be included in this study as they are easier to interpret in the context of sport-related events and using video footage retrospectively. The brain regions associated with impacts seizures from concussive impacts are not described in the literature. Consequently, the brain regions were inferred from literature pertaining to severe traumatic brain injury.

The impact seizures observed in this thesis are similar in presentation to cases of abnormal posturing in traumatic brain injuries described by Bricolo et al. (1977) in which they examined 800 patients with severe head injuries, with the exception for the duration of the coma and the posturing. They reported that 39.6% of head injuries presented with some type of decerebrate posturing and described the following types of abnormal posturing:

Full decerebrate rigidity: 34.4% of cases involved clenching of the jaw and extension of the four limbs (the upper limbs more than the lower) with the arms adducted and internally rotated accounting for 34.4% of their cases.

Unilateral decerebrate rigidity: 11.7% of posturing cases were described as unilateral with the features of the full decerebrate posturing present on only one side of the body.

Decorticate rigidity: 6.6% of patients with posturing exhibited a triple flexion of the upper limbs and clenched fists, while the lower limbs were hyperextended.

Combined decerebrate rigidity: this type of posturing was described as being more complex with one side of the body in extension and the other in flexion and was present in 6.3% of posturing cases.

Mixed decerebrate rigidity: This posturing is described as hyperflexion of the lower limbs and hyperextension of the upper limbs and occurred in only 1.6% of cases. This type of posturing was described as more closely associated in reaction to pain as opposed to the maintained posture associated with the other types of posturing.

Alternating decerebrate posturing: The most frequently observed posture (39.4%) was comprised of a variable posturing attitude consisting of either flexor or extensor posturing of the same limb, either spontaneously following the injury or in reaction to pain.

The brainstem, cerebral white matter, thalamus, cerebral cortex, and cerebellum have been suggested to be involved in the production of abnormal posturing.

Brainstem

It was hypothesized that abnormal posturing was caused by lesions of the suppressor region of the bulbar reticular formation leading to an impairment of the equilibrium between facilitatory and inhibitory activity leading to an unopposed action of the facilitatory action of the pontine tegmentum resulting in overactivity of spinal mechanism manifested by abnormal posturing (Magoun, 1944; Rhines & HW, 1946). This hypothesis was tested and supported by Ward (1946), who showed that abnormal posturing can be induced by sodium cyanide or lesions in the reticular formation and be prevented when severing the facilitatory region of the pontine tegmentum.

This is consistent with the findings from Bricolo et al. (1977) who performed autopsies on 31 of their posturing patients. Evidence of macroscopic damage of the brainstem consisting of hemorrhage and/or foci of softening of tissue was observed in 14 out of 17 of patients with full decerebrate posturing, five out six patients with alternating decerebrate posturing, two out of three patients with combined decerebrate posturing, and in the one patient with unilateral decerebrate posturing and the one with mixed decerebrate posturing (Bricolo, Turazzi, Alexandre, & Rizzuto, 1977). This suggests that the brainstem is involved regardless of the type of abnormal posture following head injuries. Unfortunately, no patient with decorticate posture was examined by autopsy. Further evidence of brainstem involvement was demonstrated by the large proportion of cases (95.5%) of abnormal posturing occurring with positive ocular signs consistent with brainstem lesions (Bricolo, Turazzi, Alexandre, & Rizzuto, 1977).

White matter and the corpus callosum

Bricolo et al. (1977) also reported that hemispheric white matter damage was often present in cases of abnormal posturing although they did not report the frequency of these observations. They did confirm lesions in the corpus callosum in 18 of the 31 cases examined by autopsy (Bricolo, Turazzi, Alexandre, & Rizzuto, 1977).

Thalamus and cerebral cortex

Thiele (1905) demonstrated that cases of posturing only occur when the brain is sectioned in the posterior part of the thalamus or deeper into the brain. On the other hand, Bricolo et al. (1977) reported lesions to more superficial brain regions with their cases of posturing describing cortical contusions and non-descript white matter abnormalities in conjunction with deeper brainstem lesions on autopsy. Decorticate posture has also been described by Davis & Davis (1982) to be the result of lesions to the cerebral cortex, the internal capsule, and the thalamus. There is also evidence of purely cortical lesions producing abnormal posturing (Langworthy, 1928; Laughton, 1928)

Cerebellum

There are some discrepancies regarding the cerebellum's involvement in abnormal posturing. It was first mentioned by Sherrington (1897) that stimulation of the anterior lobe of the cerebellum could inhibit decerebrate rigidity, suggesting that a dysfunction of this region could be the cause. However, it was demonstrated that complete removal of the cerebellum had either no effect (Sherrington, 1906; Pollock & Davis, 1930) or resulted in abolition of abnormal posturing (Miller & FG, 1922; Weed, 1914). In conjunction with lesions to the regions aforementioned, Bricolo et al. (1977), also reported evidence of damage to the cerebellum in their autopsies. As a result, the role of cerebellar lesions in abnormal posturing is still not clear.

<u>Summary</u>

Similar brain regions are proposed for both LOC and abnormal posturing, yet they are two separate signs of injury. It is unknown what creates this difference. Although, there is little literature on the brain regions associated with impact seizures, the studies examining the macroscopic injuries associated with abnormal posturing in traumatic brain injuries describes concomitant lesions to multiple brain regions. (Bricolo, Turazzi, Alexandre, & Rizzuto, 1977;

Davis & Davis, 1982). This suggests that a large volume of the brain might be affected with this type of concussive presentation. The most commonly reported regions for both types of clinical presentation are the brainstem and the thalamus. Deep structures of the brain such as the brainstem typically require a greater force of impact ((Lighthall, 1988; Gennarelli, et al., 1982). This would suggest that both loss of consciousness and impact seizures would require a greater severity of impact than concussions without these signs.

The severity of impacts associated with concussions with loss of consciousness or impact seizures is poorly described in the literature. The understanding of the relationship between impacts and resulting brain tissue trauma associated with these signs of concussions could lead to changes in management protocols or rules aiming at decreasing their incidence. Physical reconstructions and finite element modeling of concussive impacts with loss of consciousness and impact seizures could further the understanding of the severity of injury associated with these signs.

Thesis objectives

Main objective: To determine the severity of impacts associated with loss of consciousness and impact seizures following head impacts in sports

Secondary objectives:

a) To determine the severity of knock-out punches in boxing (Study One)
b) To determine the severity of loss of consciousness in American football concussive impacts (Study Two)
c) To determine the differences in biomechanical parameters between cases of concussions with loss of consciousness and cases of concussions with impact seizures (Study Three)

PART II

Study One

Brain trauma associated with punches resulting in loss of consciousness in boxing

Abstract

Objective: To compare the head dynamic response and the brain tissue deformation (maximum principal strain, cumulative strain damage measure-10%, and strain rate, between LOC and non-LOC punches in boxing.

Methods: A video analysis was performed to document the types of punches that resulted in a loss of consciousness and establish the four most common punches that did not result in loss of consciousness. Impact representations were conducted using a high velocity impactor and an anvil impacting a hybrid III headform to replicate each punch and obtain the linear and rotational acceleration-time curves. The Wayne State University Brain Injury Model was used to obtain MPS, CSDM10, and SR in the cerebral cortex, the cerebral white matter, the brainstem, the thalamus, and the corpus callosum.

Results: A hook directed perpendicularly at the mandibular angle was confirmed as the most common punch resulting in loss of consciousness. Peak linear and rotational acceleration were significantly greater for punches with loss of consciousness than those with no loss of consciousness. LOC punches resulted in significantly greater MPS in all the brain regions, CSDM10 in all the brain regions with the exception of the brainstem and strain rate in the cerebral cortex, the cerebral white matter and the brainstem.

Conclusion: High energy hooks to the mandibular angle have a high likely hood in resulting in a loss of consciousness. These punches are associated with greater magnitudes of brain trauma reflected in the high magnitudes of rotational acceleration produced with this type of punch.

Key words: Boxing, biomechanics, loss of consciousness, brain trauma

Introduction

The Association of Ringside Physicians recently published a consensus statement on concussion management in combat sports.[1] There are minor differences between their recommendations and those from the consensus statement on concussion in sport issued from the 5th international conference on concussion in sport.[2] One important difference is an emphasis on a delayed return to sport after a knockout (KO) with a loss of consciousness (LOC) in combat sports. The Association of Ringside Physicians recommend that athletes who have lost by KO with loss of consciousness as a result of a head blow be suspended for a minimum of 90 days. This is different from the consensus statement on concussion in sports as the latter does not account for LOC once a severe traumatic brain injury has been ruled out.[2] Although LOC was used as an indicator of severity of concussive injury in the past, it no longer is due to the ambiguity of research regarding LOC and its severity. The conflicting literature on severity of concussive injury with LOC makes the establishment of a return to sport protocol challenging for these subset of athletes.

Scientists have reported an association between LOC and delayed recovery in sports suggesting that LOC may be indicative of a more severe injury.[3-5] In contrast, the vast majority of researchers have failed to find a link between the presence of LOC and difference in performance on neuropsychological testing,[6-10] which suggests that there is no association between LOC and cognitive impairment. Early studies in biomechanics suggested that a loss of consciousness was caused by greater magnitudes of brain tissue deformation or to deformation of deeper and more vulnerable parts of the brain.[11] However, this research was conducted on anesthetized animals and the results were not readily generalizable to human concussions. The relationship between head impacts that lead to loss of consciousness and those that do not is poorly understood.

Laboratory impact representations and finite element modeling of head impacts can provide the necessary knowledge to further the understanding of the severity of head impacts with loss of consciousness. Finite element modeling of impacts allows for the calculation of brain tissue strains and could provide information on the severity of head impacts with loss of consciousness. This in turn could provide an indication of severity and inform clinicians with return to sport guidelines.

Metrics obtained using this method include peak linear and rotational acceleration, maximum principal strain (MPS), cumulative strain damage measure 10% (CSDM10) and strain rate (SR). Previous research have demonstrated that these metrics correlate well with concussive injuries for several regions of the brain,[12-17] demonstrating that this method is sensitive enough to establish severity.

The purpose of this study was to use laboratory impact representations to compare the magnitudes of head dynamic responses (peak linear and rotational acceleration) and brain tissue deformation (MPS, CSDM10, SR) in the cerebral cortex, the cerebral white matter, the brainstem, the thalamus and the corpus callosum between representations of common head impacts that lead or do not lead to LOC in boxing to provide a better understanding of the severity of head impacts causing a loss of consciousness.

Methods

Video analysis

Video analysis of boxing videos was conducted to identify trends in types of punches that lead to a loss of consciousness. Four hundred boxing matches were evaluated for the following criteria: 1) the match was decided by KO and 2) the KO resulted in a loss of consciousness described by a total loss of motor tone and/or evidence of posturing (flexor and/or extension behavior, fencing, impact seizures) following an impact and the inability of the boxers to protect themselves in the ensuing fall. 31 cases were identified to match these criteria. Twenty- eight of the cases were the result of a hook perpendicular to the mandibular angle, 2 were caused by uppercuts perpendicular to the same location (the receiving boxers had their head turned to the side in a combination of cervical rotation and flexion), and the last one was caused by a hook in a location slightly higher than the mandibular angle. Therefore, in the videos analyzed, the most common mechanism leading to LOC was a hook perpendicular to the mandibular angle (figure 4).

***Figure 4**. Example of a hook perpendicular to the mandibular angle*

Videos were also analyzed to characterize the impact conditions in boxing that do not lead to LOC. Twelve 3-minute rounds resulting in judges' decision matches were viewed to determine the impact locations representative of non-KO punches. The 12 rounds were divided into 4 matches to eliminate the boxer's preference for target locations. To eliminate fatigue bias, each match was comprised of a different set of rounds (match 1= round 1-3, match 2= round 4-6, match 3= round

7-9, match 4= round 10-12). A reference grid system using similar to previously published impact location grid in boxing was used to describe the locations of front and side impacts.[18]

Impacts to the front of the head are characterized by a wide range of impact conditions (impact location X impact angle) mostly due to the combination of 4 different types of punches (jab, cross, hook, and uppercut) and the boxers ability to avoid punches. To account for this variability, the reference grid for the facial impacts was further divided into 9 areas, each with four possible impact vectors: 1) directly from the front, 2) directly from the side, 3) from the right at an angle between front and side, 4) from the left at an angle between front and side for a total of 36 possible impact conditions. Figure 5 displays the impact location associated with LOC punches and the reference grid used to characterize the non-LOC punches in boxing.

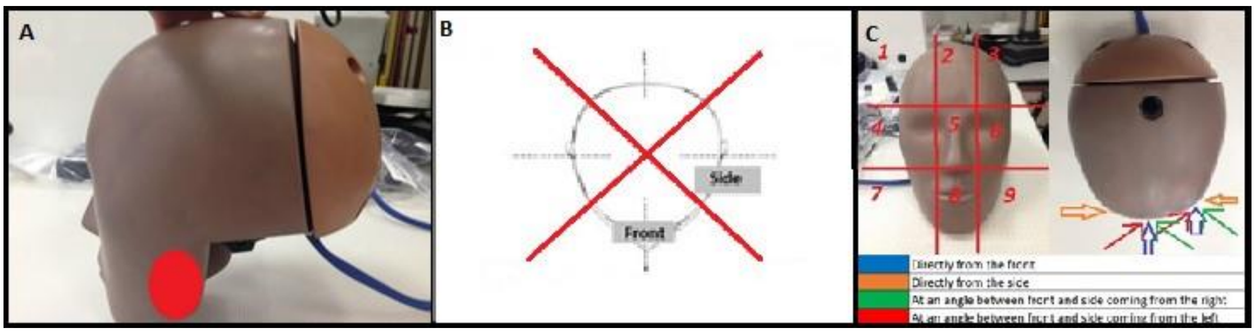

Figure 5. *A) Impact location associated with LOC punches. B) References grid defining frontal and side impacts. C) Reference grid used to characterize the frontal impacts.*

Impacts to the side of the head are far less complex. They are the results of hooks since the nature of the jab, cross and uppercut does not lead to impact towards the side of the head. The side area was divided in three parts longitudinally to establish a top, middle and bottom section. Impacts to the back of the head are considered illegal in boxing and were not included in this analysis.

In total, 380 impacts were recorded during 12, 3-minute rounds, for an average of approximately 15 impacts per 3-min round per boxer. The impact frequency of was consistent with previous research that reported an average of 10.5 impacts per round for four 2-minutes rounds.[18]

Impacts to the face represented 68% of all impacts. Despite the 36 possible impact conditions, 2 conditions represented the majority of impacts: frontal impact to area 2 (centre of the forehead) and 5 (nose) represented 22% and 26% of frontal impacts respectively.

Impacts to the side represented 27% of all impacts. The most common location was the middle section (26% of side impacts) and were the results of a hook aimed towards the mandibular angle while the receiving boxer was either turning (contralateral rotation of the head) or leaning (contralateral lateral flexion) away from the incoming punch. Therefore, four impact conditions not resulting in LOC were identified as: jabs to the nose, jabs to the forehead, hooks to side of the head while the receiving boxer is turning away, hooks to the side of the head while the receiving boxer is leaning away.

Impact representation

Typically, physical reconstructions and finite element modeling of impacts would be performed to compare the brain tissue deformation associated with these types of impacts. Unfortunately, boxing ring dimensions are not consistent but vary across arenas, which means that accurate impact velocity was challenging to calculate from video recordings.

Representations of the common impacts can be used to identify the magnitudes of brain tissue deformation of punches that either result in LOC or no LOC. The impact locations identified in the video analysis were impacted at velocities, and striking masses cited in literature and consistent with the type of punches represented. The compliance of jabs and hooks was determined using experienced boxer hitting the hybrid III headform.

Equipment

Impact representations were conducted using a high velocity impactor. The HVI consists of a 3.35 meter-long dual rail system mounted on a steel frame. It is attached to 4000-pound ETV winch that adjusts for height and angle of projection. A carriage attaches onto the rails with wheels, and is accelerated by two wheels propelled by a 2.2 kW electrical motor. The launching velocity is adjustable by a RPM controller. The impact velocity is measured by a photoelectric time gate located just prior to impact. At the end of the rails, there is a 15-cm thick piece of VN foam causing the anvil to be released and launched towards a fixed headform.

Releasable anvil

The carriage holds an anvil that mimics the mass and compliance of a human fist. The point of attachment between the releasable anvil and the carriage are low friction bushings to allow the anvil to be launched with a consistent velocity. The mass of the releasable anvil can be adjusted from 2.3 to nine kg to replicate the striking mass in a human subject.[19]

Procedures

Each impact event (1 KO, 4 non-KO) was reconstructed at three velocities (low, medium, high) and two masses (low, high) consistent with boxing impacts described in the literature (Table

8). Viano et al. (2005b) and Stojsih (2008) both reported an average of 11 m/s hand velocity for hook impacts. Jabs and unspecified punches in the frontal area of the face were reported to be approximately 9 m/s.[18-20] The upper and lower velocities were selected by constructing 99% confidence interval around the mean velocities described in the literature. The masses of the boxers included in the 31 cases of LOC in this research ranged from 55 to 106 kg. Striking masses for flyweight (50 kg) and super heavy weight (108 kg) of 2.31 kg and 4.97 kg respectively were reported in previous research.[19] The striking masses used in this study were selected to represent the mass associated with the lowest and highest weight classes in boxing and obtain a range of possible responses for the fighters that induced a loss of consciousness to their opponent in the video analysis.

Impact parameters	**Description of the value used**	**Value used**	**Source**
Impact Velocity	Mean and 99% CI	Hooks: 11±1.5 m/s Jabs: 9±1.5 m/s	(Stojsih, Boitano, Whilelm, & Bir, 2008)[18]
Striking mass	Mean for weight class	Flyweight: 2.33 kg Super heavy weight: 4.78 kg	(Walilko, Viano, & Bir, 2005)[19]

Table 8. *Impact parameters used for impact representations of hooks and jabs.*

The compliance associated with boxing punches is not reported in the literature, and as a result established by having experienced boxers hitting the hybrid III headform with hooks and jabs to represent the types of punches observed in the video analysis. Seven boxers were asked to hit the headform three times with a jabs to the forehead and three times with a hook to the side of the headform with a 10-oz boxing glove to obtain the acceleration-time curves for linear and rotational acceleration. Then the releasable anvil was fitted with a 10-oz boxing glove and vinyl nitrile (VN) foam to replicate the acceleration-time curves obtained from the boxers. The compliance of the jabs were best represented with a combination of a 10-mm VN 1000 and a 10-mm VN 760. The hooks were best represented with a combination of a 20-mm VN 1000 and a 5-mm VN 600. In addition to the VN foam, the anvil was fitted with a 10-oz boxing glove for both jabs and hooks. Figure 6 and 7 display the mean curves for jabs and hooks obtained from experienced boxers with a 95% confidence interval as well as the curves obtained using the laboratory anvil.

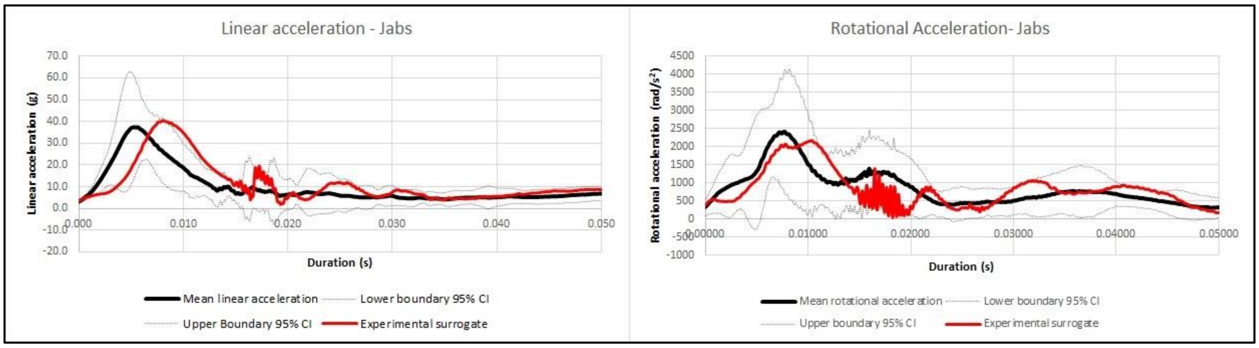

Figure 6. *Mean linear (left) and rotational (right) acceleration-time curves associated with jabs in boxing.*

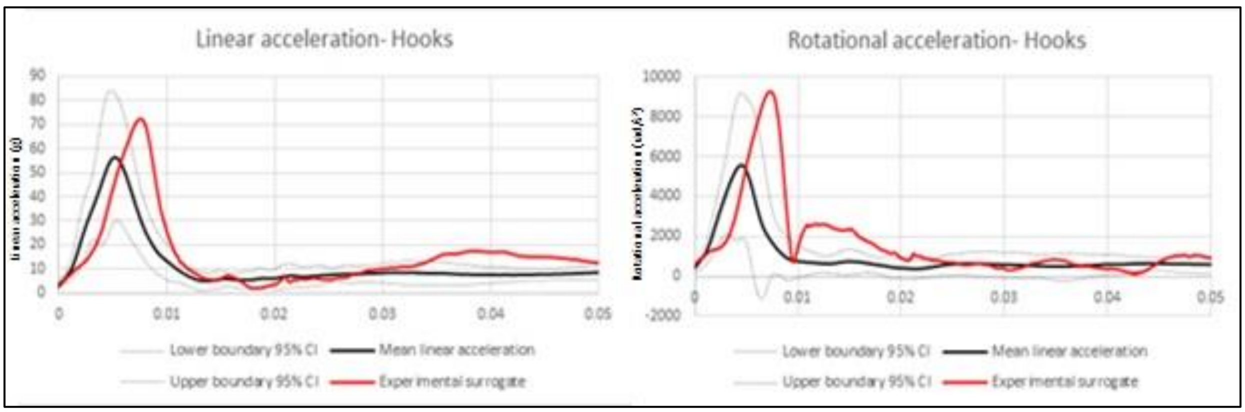

Figure 7*. Mean linear (left) and rotational (right) acceleration-time curves associated with hooks in boxing.*

The releasable anvil impacted the hybrid III headform fitted with 9 accelerometers in 3-2-2-2 array [21] mounted on an unbiased neckform.[22] DTS TDAS Pro software sampled at 20 kHz and was used to obtain acceleration-time curves. The data was filtered at 1000 Hz according to the SAE J211 convention. The resulting acceleration curves were input into the Wayne State University Brain Injury Model (WSUBIM) [23] to calculate maximum principal strain (MPS), cumulative strain damage measure at 10% (CSDM10) and strain rate in the cerebral cortex, white matter, the corpus callosum, thalamus and brainstem. The model was validated for pressure and brain motion as described by Zhang et al.[23]

Statistical analysis

Independent sample t-tests were performed for each variable to compare the magnitudes of LOC punches to the magnitudes of the four most common non-LOC punches.

Results

The magnitudes of peak linear and rotational acceleration were significantly higher for the LOC punches when compared to the non-LOC punches. The magnitudes of maximum principal strain were significantly greater in all the brain regions analyzed in this study for the LOC punches. Similarly, the cumulative strain damage measure at 10% yielded statistically greater volume of strain in all the brain regions analyzed with the exception of the brainstem. The strain rate was statistically higher in the cerebral cortex, the cerebral white matter and the brainstem but not in the thalamus or the corpus callosum. The magnitudes of peak accelerations, MPS, CSDM10, and strain rate of KO and non-KO punches, and p-values are provided in Tables 9-12.

Kinematic Variables			
	LOC punches	Non-LOC punches	P-value
Linear acceleration	123.3 ± 65.3	68.6 ± 42.7	0.003
Rotational acceleration	11279.5 ± 4743.1	6145.5 ± 4523.5	<0.001

Table 9*. Mean of kinematics variable of knock-out punches and non-knock-out punches and results of the independent sample t-tests. Statistically significant results are displayed in* ***bold.***

Maximum Principal strain			
Brain region	LOC punches	Non-LOC punches	P-value
Cerebral Cortex	0.73 ± 0.16	0.47 ± 0.21	< 0.001
Cerebral White Matter	0.69 ± 0.12	0.38 ± 0.17	< 0.001
Brainstem	0.44 ± 0.09	0.34 ± 0.15	0.001
Thalamus	0.36 ± 0.07	0.28 ± 0.14	0.028
Corpus Callosum	0.45 ± 0.07	0.32 ± 0.18	0.004

Table 10. *Mean of maximum principal strain (MPS) of knock-out punches and non-knock-out punches and results of the independent sample t-tests. Statistically significant results are displayed in* ***bold.***

Cumulative Strain Damage Measure-10%			
Brain region	LOC punches	Non-LOC punches	P-value
Cerebral Cortex	0.81 ± 0.19	0.45 ± 0.28	< 0.001
Cerebral White Matter	0.88 ± 0.05	0.33 ± 0.27	<0.001
Brainstem	0.32 ± 0.21	0.23 ± 0.25	0.16
Thalamus	0.90 ± 0.13	0.37 ± 0.34	<0.001
Corpus Callosum	0.91 ± 0.08	0.41 ± 0.31	<0.001
Entire Brain	0.81 ± 0.13	0.38 ± 0.27	<0.001

Table 11. *Mean of Cumulative Strain Damage Measure at 10% (CSDM10) of knock-out punches and non-knock-out punches and results of the independent sample t-tests. Statistically significant results are displayed in* ***bold.***

Strain Rate (s^{-1})			
Brain region	LOC punches	Non-LOC punches	P-value
Cerebral Cortex	124 ± 36	76 ± 39	<0.001
Cerebral White Matter	111 ± 27	75 ± 43	0.001
Brainstem	82 ± 16	67 ± 39	0.019
Thalamus	54 ± 15	57 ± 36	0.499
Corpus Callosum	77 ± 14	64 ± 47	0.079

Table 12. *Mean of Strain Rate of knock-out punches and non-knock-out punches and results of the independent sample t-tests. Statistically significant results are displayed in* ***bold.***

Discussion

Severity of head impacts leading to loss of consciousness

The results of this study demonstrate that punches that lead to loss of consciousness in boxing are associated with greater magnitudes of head dynamic responses which resulted in greater brain tissue trauma than the non-LOC punches. Depending on the metric used, all the brain regions analyzed in this study resulted in greater brain tissue deformation. This suggests that boxing impacts that lead to LOC are more severe than non-LOC punches and supports the notion that a delayed return to sport may be beneficial for these fighters.

The greater brain tissue deformation associated with these type of punches is likely due to a combination of the impact location and striking velocities which are associated with greater peak rotational acceleration. Impact locations away from the center of gravity are associated with greater magnitudes of rotational acceleration and greater brain tissue deformation.[24,25] Furthermore, greater striking velocities are also associated with greater peak acceleration and greater magnitudes and depth of brain tissue deformation.[26,27]

Video analysis of boxing knock-outs

The video analysis performed in this study confirmed than a hook to the mandibular angle is the prime mechanism for loss of consciousness in boxing. More than a quarter of all punches observed were hooks directed at the side of the head. One remarkable observation from the video analysis was that some of the hooks to the side of the head were directed and made contact with the mandibular angle but did not induce loss of consciousness. In these instances, the boxer receiving the hit used a defensive strategy to decrease the amount of the energy being transfer to the head. The three most common strategies were partially blocking the incoming punch, leaning away or looking away from the incoming punch. Interestingly, whenever a high-energy hook was directed perpendicularly at the mandibular angle and no strategies were used, it indubitably resulted in a loss of consciousness. This is probably due to the nature of the hooks. Hooks are associated with greater velocities and greater punch forces than other common punches,[18] and are likely to allow for a greater energy transfer to the brain. In addition, hooks to the side of the mandibular angle resulted in high values of rotational acceleration in more than one plane which has been reported to increase the resulting brain tissue strain.

This represents a unique opportunity for combat sports governing bodies to reduce brain trauma in lower levels of competition. Banning hooks in competition would result in a significant decrease in LOC incidence but also could decrease the overall brain trauma sustained by the fighters.

Limitations

Impact velocity and mass were obtained from the literature to represent the appropriate punch conditions analyzed in this study. Brain tissue trauma associated with hooks to the mandibular angle were compared to four other common punches in boxing. Laboratory impact representations are beneficial in understanding the interactions between impact parameters and the resulting brain tissue trauma.

The hybrid III headform is a representation of a 50th percentile male primarily designed to be used in automobile accidents and may not capture subtle differences in the kinematics of the head following head impacts from punches. The Wayne State University Brain Model (WSUBIM) was validated against skull fracture, intracranial pressure and brain motion analysis; though, the correlation to brain motion was limited and the validation was not conducted in every brain regions analyzed in this study.[23] The strain values obtained by FEMs is an approximation based on the mechanical properties attributed to the different types of tissues, the boundary conditions, the mesh density and the shapes of the elements. It is unlikely that these limitations had an effect on the results of the comparisons between hooks to the mandibular angle and the other types of punches since the WSUBIM is sensitive enough to differentiate between cases of concussions and cases of head impacts that did not lead to injury in sports.[16,26]

Conclusion

The video analysis performed in this study confirmed that a hook delivered perpendicularly to the mandibular angle is the prime mechanism of loss of consciousness in boxing. The impact representations performed in laboratory demonstrated that these punches are associated with a greater magnitudes of brain tissue trauma. This supports the notion that fighters who have lost by knockout with a loss of consciousness could benefit from a longer recovery period before being allowed to resume fighting activities.

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Study Two

Biomechanical comparison of concussions with and without a loss of consciousness in elite American football: Implications for prevention

Abstract

Loss of consciousness (LOC) associated with concussion is no longer considered an indicator of severity of injury in current concussion management protocols. Studies investigating the association between LOC and recovery time or neurophysiological performance have reported ambiguous findings and resulted in a limited understanding of the severity of LOC-inducing head impacts. Concussive injuries with and without LOC from helmet-to-helmet and shoulder collisions and falls in elite American football were reconstructed in laboratory using a hybrid III headform and finite element model to obtain peak linear and rotational acceleration and brain tissue deformation metrics in the cerebral cortex, the cerebral white matter, the corpus callosum, the thalamus and the brainstem. Impact velocity, peak linear and rotational acceleration were significantly greater in the LOC group than the no LOC group. The brain tissue deformation metrics were greater in the LOC group than the no LOC group. The best overall predictor for loss of consciousness was impact velocity. Concussions with LOC are characterised by greater magnitudes of brain tissue deformation. This was mainly the result of higher impact velocities in the LOC group providing league decision-makers with an understanding of the importance of managing impact velocity through athlete education and rule enforcement.

Key Terms: Concussions, Biomechanics, Loss of consciousness, Severity

Introduction

It is estimated that eight percent of concussions in the National Football League result in a loss of consciousness (LOC) (Casson, Viano, & Pellman, 2010). The role of LOC as an indicator of severity is ambiguous. Casson et al. (2010), reported that the proportion of American football players who took longer than 14 days to return to play following a concussion is approximately four times as many players who lost consciousness (25.9%) than players who didn't (5.9%) (Casson, et al, 2010). Loss of consciousness has been associated with a prolonged recovery in professional ice hockey as well as in high school and collegiate sports (Benson, Meeuwisse, Rizos, Kang, & Burke, 2011; Guskiewicz, Weaver, Padua, & Garrett, 2000; McCrea, et al., 2013). In contrast, researchers also report no link between LOC and the duration of symptoms or the risk for persistent post-concussion syndrome (Elbin, & Collins, 2013; Erlanger, et al., 2003; Meehan, Mannix, Stracciolini; Morgan, et al., 2015; Zemek, et al., 2016;). LOC is also considered an indicator of severity when clinicians attributed grade to concussions, i.e. higher grades of concussion were determined by longer duration of LOC (Cantu, 1986; Kelly, Nichols, Filley, Lillehei, & Kleinschmidt-DeMasters, 1991). Recently clinicians have moved away from concussion grades and currently, LOC is considered a sign to send an athlete to the emergency department following a head impact (McCrory et al., 2017). This limited understanding of what LOC represents led to concussion management protocol that does not account for loss of consciousness once a severe traumatic brain injury has been ruled out. An objective measure of impact severity would provide the information needed to address a loss of consciousness following a concussive impact and understanding how it occurs can help develop prevention strategies in sports.

Physical reconstructions of head impacts have been used to study the biomechanics of concussive injuries in sports (Viano, Casson, Pellman, King, & Yang, 2005; Zhang, Yang, & King, 2004, Post, et al, 2015, Hoshizaki et al, 2017). Researchers have used peak linear and rotational acceleration to measure the risk for injury to distinguish between cases of concussions and cases of no-injury when isolating for the type of event causing the injury (Pellman, Viano, Tucker, Casson, & Waeckerle, 2003; Zhang, et al., 2004). The type of event (collisions, falls, or projectile) is characterised by the impact velocity, impact location and/or direction, striking mass and compliance. These four factors interact to create unique shapes of acceleration curves (Figure 8) (Karton, Hoshizaki, & Gilchrist, 2014; Goodman, Cherian, Bryan, & Robertson, 1994; Gurdjian, Roberts, & Thomas, 1966; Zhou, Khalil, & King, 1997), making it difficult to compare across types of events using variables such as peak linear and rotational acceleration.

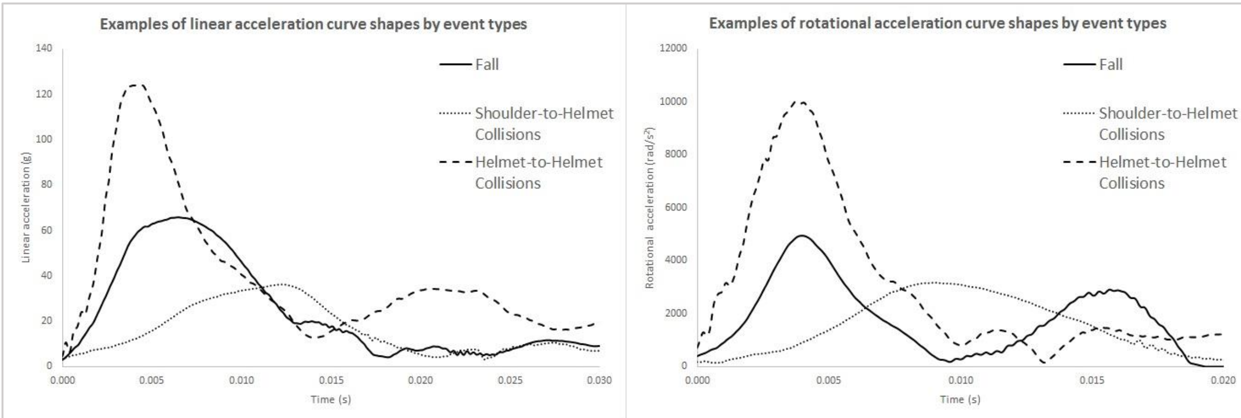

Figure 8. *Examples of linear (left) and rotational (left) acceleration time curves for different types of impact events.*

Finite element brain models are used to estimate the values of strain-based measure associated with head impacts (Kleiven, 2007; Patton, McIntosh, & Kleiven, 2013; Viano, et al, 2005). Maximum principal strain (MPS), cumulative strain damage measure (CSDM), and strain rate for chosen brain regions can be obtained using this method. MPS, CSDM at 10%, and strain rate have been positively associated with concussive injuries in several regions of the brain (Kleiven, 2007; Patton, et al., 2013; Patton, McIntosh, & Kleiven, 2015). Strain rate has been reported to correlate with LOC in American football in a small sample of four cases (Viano, et al., 2005). The relationship between MPS and CSDM at 10% with LOC has not been investigated; however, given their good correlation with concussive injury, it would be important to confirm this relationship with a larger sample.

The brainstem and thalamus are integral parts of normal consciousness. Research with traumatic brain injuries (TBIs) patients reported that lesions in these two brain regions are associated with deep coma (Gentry, Godersky, & Thompson, 1988; Levin, et al., 1988; Levin, et al., 1997). Imaging studies have reported LOC from TBI could result from isolated lesions to any of these structures: the cerebral cortex, the cerebral white matter, the thalamus and the brainstem and the duration of the coma was associated with the depth of the lesion demonstrating the importance of deep brain structure in relation to consciousness. (Gentry, et al, 1988; Levin, et al. 1988; Levin, et al. 1997). Gennarelli et al. (1982) demonstrated that diffuse axonal injury in the corpus callosum from lateral impacts was associated with traumatic coma of longer duration. Gentry et al. (1988) showed that injury to the corpus callosum was associated with greater alteration in consciousness as measured by the Glasgow Coma Scale (GSC). However, lesions to the corpus callosum are often associated with lesions in the brainstem which may play an influential role in a loss of consciousness (Adams, Graham, Murray, & Scoot, 1982; Gennarelli, et al., 1982; Gentry, et al., 1988). Kleiven (2007) demonstrated that these regions could differentiate between cases of injury and no-injury head impacts in a sample of professional American football head impacts using laboratory reconstructions and finite element modeling, suggesting that this method and these brain regions might be sensitive enough to differentiate between cases of concussions with and without LOC.

Energy delivered to the brain is one of the most influential factor in provoking trauma to the deeper structures to the brain (Lighthall, 1988; Yan, Johnstone, Alwis, Morganti-Kossman, & Rajan, 2013). It was hypothesised that concussions with LOC are likely the result of high energy impacts creating brain tissue deformation in the deeper structures of the brain and therefore more severe injuries than concussions without LOC.

The purpose of this study was to compare the cases of concussions with and without LOC in elite American football players using head accelerations and brain tissue deformation in the cerebral cortex, cerebral white matter, corpus callosum, thalamus and brainstem.

Methods

Case selection

All cases included in this study were concussions that occurred in the National Football League for which a press release was issued confirming that the player had received a concussion diagnosis by the team's medical team between 2009 and 2014. Publicly available videos of the injurious impacts were watched to classify athletes based on the injury status. The following inclusion criteria were used to determine the cases of concussion with loss of consciousness for video analysis. For concussions caused by a collision (shoulder to the head or helmet to helmet impact), the injured player had to display a complete loss of motor tone, a failure to protect themselves during the ensuring fall or display a body position exhibiting characteristic of flexor or extensor posturing, sometimes referred to as abnormal posturing, impact seizure or fencing response (Hosseini & Lifshitz, 2009; McCrory, Bladin, & Berkovic, 1997; McCrory & Berkovic, 2000). For fall events, cases in which the athlete rebounded from the first impact and displayed the same criteria applied for the collision injuries were included in this study. Every case of concussion that matched these criteria were included in this study as part of the LOC group.

Cases of non-LOC concussion were divided based on the event that lead to the concussion (fall, shoulder or helmet-to-helmet collisions) and a random number generator was used to select which cases would be included in this study. The number of injury per event were matched to the LOC group to ensure the homogeneity of the two groups.

Video analysis

Video analyses of the injury events were performed to obtain the necessary information to conduct the laboratory reconstructions. This includes the velocity at which the impact occurred, the impact location, and the type of helmet worn by the injured athlete. The videos were captured using WM Capture 8 (WM Recorder, California, USA) from publicly available media at a frame rate of 25 fps as described by Post et al. (2018), and their resolution of 1896 x 1016 pixels. The impact velocity was determined using Kinovea (0.8.20) [Appendix B2] by applying a calibration grid on the field and measuring the distance between the two players' helmets at a set time prior to the impact for collisions cases. The distance prior to impact was measured at a set time ranging between 0.04 and 0.20 second (1 to 5 frames) (Post, et al., 2018). The time was determined when the players were maintaining a constant velocity prior to the impact. For falling injuries, the horizontal component of velocity was calculated using a calibration grid measuring the horizontal distance traveled 0.08 seconds prior to the impact. The vertical component was calculated by measuring the height from the ground at 0.04 second prior to the impact using a known vertical distance such as the width or the length of the injured player's helmet.

Velocity calculation using video analysis requires additional criteria: 1) The head of the player must be visible at the moment of impact and at the required time frame 2) Known markers on the field such as hash mark or lines must be visible in the frame chosen to measure the distance prior to the impact and 3) It must be possible to establish a calibration grid in the general orientation of the impact. This method of measuring impact velocity has been reported to have an error of less than 10% in ice hockey and intra and inter-rater reliability of 0.96 and 0.958 respectively (Post, et al., 2018). In this study, the intra-rater reliability was 0.96. The measurement error for using this method in American football has not been investigated. However, the error in ice hockey stems from the distance of the calibration in relation to where the impact occurred. In football, it is possible to lay the calibration grid directly where the impact occurs, minimizing this type of error. Therefore, the measurement error for impact velocity in American football should be similar or less when compared to ice hockey.

In total, 5 falls, 21 helmet-to-helmet collisions and 15 shoulder collisions were reconstructed in each of the injury groups for a total of 82 injury reconstructions.

Impact reconstructions

Laboratory impact reconstruction were performed to obtain the kinematics of the head including peak linear and rotational acceleration and acceleration-time curves to input into a finite element model of the brain. The three-dimensional linear and rotational accelerations were collected using a hybrid III 50^{th} percentile headform mounted on an unbiased neck that allow for similar movement in all plane of motion (Walsh, Kendall, Post, Meehan & Hoshizaki, 2018). The hybrid III headform was equipped with nine Endevco 7264-C-2KTZ-2-300 accelerometers (Endevco, California, USA) in a 3-2-2-2 array (Padgaonkar, 1975) and sampled at 20 kHz. The acceleration data was collected using DTS TDAS system and was filtered using a CFC class 1000 filter according to the SAE J211 convention for head impact data.

Collisions

Helmet-to-helmet and shoulder-to-head collisions were reconstructed using a pneumatic linear impactor. The pneumatic linear impactor consisted of a sliding table, a frame and an impacting arm. The impacting arm equipped with a surface best representative of the injury condition is propelled horizontally by compressed air to impact a headform placed on the sliding table. The impacting arm of mass 15.9 kg was equipped with a hybrid III headform wearing an American football helmet to represent helmet-to-helmet cases (total mass of 24.0 kg). The shoulder collisions cases were done using a 13.1 kg impacting arm with 0.142 m thick VN 602 foam and an American football shoulder pad (Rousseau, 2014). The impact velocity is measured using a photoelectric time gate placed within 0.02 m of the impact (Figure 9 A and B).

Falls

Reconstruction of injuries caused by falls were done using a monorail drop rig (Figure 9 C). It consisted of a drop carriage attached to a 4.7 m l rail. The carriage is equipped with ball bushing to reduce the effect of friction. The carriage is released by a pneumatic piston once it has reach the height required to achieve the desired impact velocity, which is measured using a photoelectric time gate place within 0.02 meter of the impact. The impacting surface consisted of a piece of artificial turf consistent with what is used in professional sport to represent the appropriate stiffness of the ground. [Appendix B4] is a summary of the cases of LOC and non LOC concussions and their impact parameters]

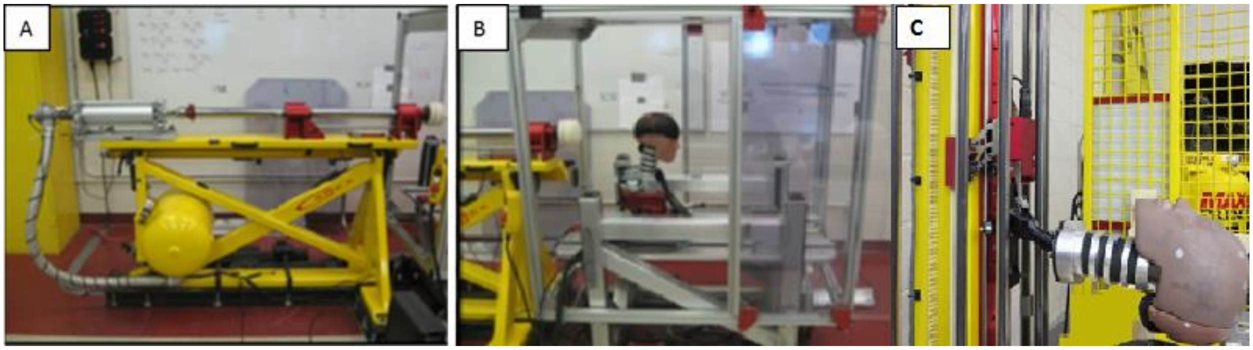

Figure 9. *A) Pneumatic linear impactor B) sliding table and Hybrid III headform C) Monorail drop rig*

The helmets used for reconstruction were matched to each case according to the material of the liner of the helmets worn by the injured players as determined by video analysis. In addition, a sufficient number of helmets were used to ensure that no helmets were impacted at the same impact location for more than one case.

Finite element modeling

The resulting linear and rotational acceleration curves were input into the Wayne State University Brain Injury Model (WSUBIM) to obtain maximum principal strain (MPS), cumulative strain damage measure above 10% (CSDM10), and strain rate in the cerebral cortex, the white matter, the corpus callosum, the thalamus, and the brainstem. The simulations were run using PAM-CRASH (ESI, Farmington Hills, MI, USA)

The WSUBIM included the skull, scalp, dura mater, pia mater, falx cerebri, falx and tentorium cerebelli, cerebrospinal fluid, lateral and third ventricles, cerebrum (grey and white matter), cerebellum, brainstem, parasagittal bridging veins, and venous sinuses for a total of 314, 500 elements (hexahedral brick and shell), and a mass of 4.5 kg (Zhang, et al., 2001). The brain tissue was modelled using a combination of a linear viscoelastic model and a large-deformation theory (Zhang, et al., 2001). The shear modulus of the viscoelastic brain was characterised as:

$G(t)=G_\infty + (G_0 - G_\infty)e^{-\beta t}$

Where G_0 is the short term shear modulus, G_∞ is the long term shear modulus and β is the decay factor (Zhang, et al., 2001). The cerebrospinal fluid layer was modelled as solid elements with a low shear modulus and was applied with a sliding but no separation condition to represent the brain skull interaction (Zhang, et al., 2001). The WSUBIM model was validated using brain motion and pressure data. The brain material properties used in the WSUBIM and a description of the validation of the model are described in Zhang et al (2001).

Statistical analysis

Independent sample t-tests were done to determine if significant differences were present between concussions with LOC and concussions without LOC for each brain region across each type of event as well as with all the events collapsed.

Logistic regressions were performed on the variables that were statistically significant in the independent sample t-tests to determine if the variables included in this study were appropriate predictors of loss of consciousness. Logistic regressions were done on individual event type and then with all the events collapsed.

Results

Kinematic variables

The t-tests revealed that concussions with LOC had significantly greater impact velocities (measured by video analysis), peak linear accelerations and peak rotational accelerations (measured from the impact reconstructions on the hybrid III headform) than non-LOC concussions for all types of events individually or together. The logistic regressions were significant for all the variables measured with the exception of the impact velocity, peak linear and rotational acceleration associated with the falls, likely due to the small sample size (n=5 per group). The means for kinematic variables and the statistical results of the t-tests and logistic regressions associated with the kinematic variables are presented in Table 13.

Kinematic variables								
Type of event	Variable measured	Mean LOC concussion (SD)	Mean Non-LOC concussion (SD)	Effect size Cohen's d	P-Value t-tests	Overall % correct classification	P-value logistic regression	Value representing a 50% risk of LOC
Shoulder collisions	Impact velocity (m/s)*	9.0 (1.1)	6.9 (1.1)	1.85	**<0.001**	73.3	**0.01**	7.95
	Peak linear acceleration (g)*	33.8 (10.1)	25.9 (4.7)	0.98	**0.012**	70.0	**0.04**	29.2
	Peak Rotational acceleration (rad/s^2)*	2996.2 (748.6)	2044 (518)	1.81	**<0.001**	83.3	**0.003**	2350
Helmet-to-helmet collisions	Impact velocity (m/s)*	9.3 (1.3)	7.2 (0.9)	1.97	**<0.001**	81.0	**0.002**	8.1
	Peak linear acceleration (g)*	91.2 (27.0)	59.7 (15.0)	1.48	**<0.001**	83.3	**0.001**	74.5
	Peak Rotational acceleration (rad/s^2)*	6496.6 (2256.4)	4522 (1081)	1.12	**<0.001**	69.0	**0.005**	4275
Falls	Impact velocity (m/s)*	5.8 (0.8)	4.0 (1.4)	1.59	**0.036**	*Logistic regression not statistically significant (n_1=n_2=5)*		
	Peak linear acceleration (g)*	103.8 (23.4)	55.6 (27.8)	1.87	**0.018**	*Logistic regression not statistically significant (n_1=n_2=5)*		
	Peak Rotational acceleration (rad/s^2)*	6505.0 (1411.8)	3228.4 (1811)	2.01	**0.013**	*Logistic regression not statistically significant (n_1=n_2=5)*		
All events collapsed	Impact velocity (m/s)*	8.8 (1.6)	6.7 (1.4)	1.35	**<0.001**	80.5	**<0.001**	7.75
	Peak linear acceleration (g)*	72.2 (36.3)	46.8 (21.4)	0.85	**<0.001**	62.2	**0.001**	57.5
	Peak Rotational acceleration (rad/s^2)*	5247.5 (2424.5)	3457.8 (1535.5)	0.90	**<0.001**	61.0	**0.001**	4300

Table 13. *Means of impact velocity (from video analysis), peak linear and peak rotational acceleration (from impact reconstructions) of LOC and non-LOC concussions, p-value of t-tests and logistic regression results. The statistically significant results are in* ***bold.***

Maximum principal strain

LOC concussions were characterized by higher MPS values when compared to non-LOC concussions in every event and in every brain region with the except for the MPS in the brainstem for fall events. Logistic regression yielded significant results for all brain regions when associated with shoulder or helmet-to-helmet collisions or when all the events were collapsed for analysis. The MPS associated with the fall events were not significant predictors. The mean MPS for each event and each brain region and the results of the t-tests and logistic regressions can be found in Table 14.

Maximum principal strain								
Type of event	Brain regions	LOC concussion (SD)	Non-LOC concussion (SD)	Effect size Cohen's d	P-value t-tests	Overall % correct classification	P-value logistic regression	Value representing a 50% risk of LOC
Shoulder collisions	Cerebral cortex	0.36 (0.07)	0.26 (0.09)	1.27	**0.002**	73.3	**0.008**	0.31
	Cerebral white matter	0.30 (0.09)	0.21 (0.08)	1.11	**0.005**	76.1	**0.021**	0.25
	Corpus callosum	0.22 (0.06)	0.14 (0.05)	1.56	**<0.001**	86.7	**0.006**	0.18
	Thalamus	0.21 (0.04)	0.132 (0.05)	1.71	**<0.001**	83.3	**0.003**	0.17
	Brainstem	0.23 (0.05)	0.16 (0.05)	1.37	**0.001**	76.7	**0.006**	0.19
Helmet-to-helmet collisions	Cerebral cortex	0.67 (0.23)	0.48 (0.15)	0.92	**0.004**	69.8	**0.013**	0.55
	Cerebral white matter	0.51 (0.13)	0.40 (0.14)	0.86	**0.007**	79.1	**0.019**	0.44
	Corpus callosum	0.42 (0.14)	0.30 (0.10)	0.99	**0.002**	65.1	**0.009**	0.35
	Thalamus	0.38 (0.13)	0.27 (0.08)	0.97	**0.003**	65.1	**0.011**	0.31
	Brainstem	0.44 (0.12)	0.32 (0.09)	1.14	**0.001**	76.7	**0.004**	0.37
Falls	Cerebral cortex	0.53 (0.11)	0.33 (0.13)	1.60	**0.036**	*Logistic regression not statistically significant ($n_1=n_2=5$)*		
	Cerebral white matter	0.46 (0.12)	0.28 (0.13)	1.53	**0.042**	*Logistic regression not statistically significant ($n_1=n_2=5$)*		
	Corpus callosum	0.40 (0.08)	0.20 (0.10)	1.34	**0.01**	*Logistic regression not statistically significant ($n_1=n_2=5$)*		
	Thalamus	0.35 (0.07)	0.19 (0.07)	2.11	**0.01**	*Logistic regression not statistically significant ($n_1=n_2=5$)*		
	Brainstem	0.36 (0.07)	0.24 (0.11)	1.34	0.067	*Logistic regression not statistically significant ($n_1=n_2=5$)*		
All events collapsed	Cerebral cortex	0.54 (0.22)	0.383 (0.16)	0.79	**0.001**	62.2	**0.002**	0.45
	Cerebral white matter	0.43 (0.15)	0.31 (0.15)	0.79	**0.001**	67.1	**0.002**	0.39
	Corpus callosum	0.35 (0.15)	0.23 (0.11)	0.89	**<0.001**	62.2	**0.001**	0.28
	Thalamus	0.31 (0.13)	0.21 (0.10)	0.90	**<0.001**	63.4	**0.001**	0.26
	Brainstem	0.35 (0.14)	0.25 (0.11)	0.85	**<0.001**	62.2	**0.001**	0.30

Table 14. *Means of MPS in the cerebral cortex, cerebral white matter, the corpus callosum, the thalamus and the brainstem, p-value of t-tests and logistic regression results for different types of impact events leading to LOC and non-LOC concussions. The statistically significant results are in* ***bold.***

Cumulative Strain Damage Measure-10%

For the shoulder collisions and all the events collapsed, the values of CSDM-10% were significantly greater in all brain regions in the LOC group compared to the no LOC group. For helmet-to-helmet collisions, only the cerebral white matter, the thalamus and brain as a whole had a significantly larger volume of strain above 10%, whereas for the falls it was the corpus callosum and the thalamus. The means and statistical results are presented in Table 15. The logistic regressions were significantly predictive for all the brain regions for the shoulder collisions. For the helmet-to-helmet collisions, only the cerebral white matter, the thalamus and the brain as a whole were predictive. With all the events collapse, the brainstem was the only brain region that did not have a statistically significant logistic regression. The small sample used for the fall events resulted in none of the brain region being predictive. Figure 10 displays the distribution of strain in the brain regions in a sagittal cross-section analyzed in this study for a case of concussion with LOC and a case without LOC.

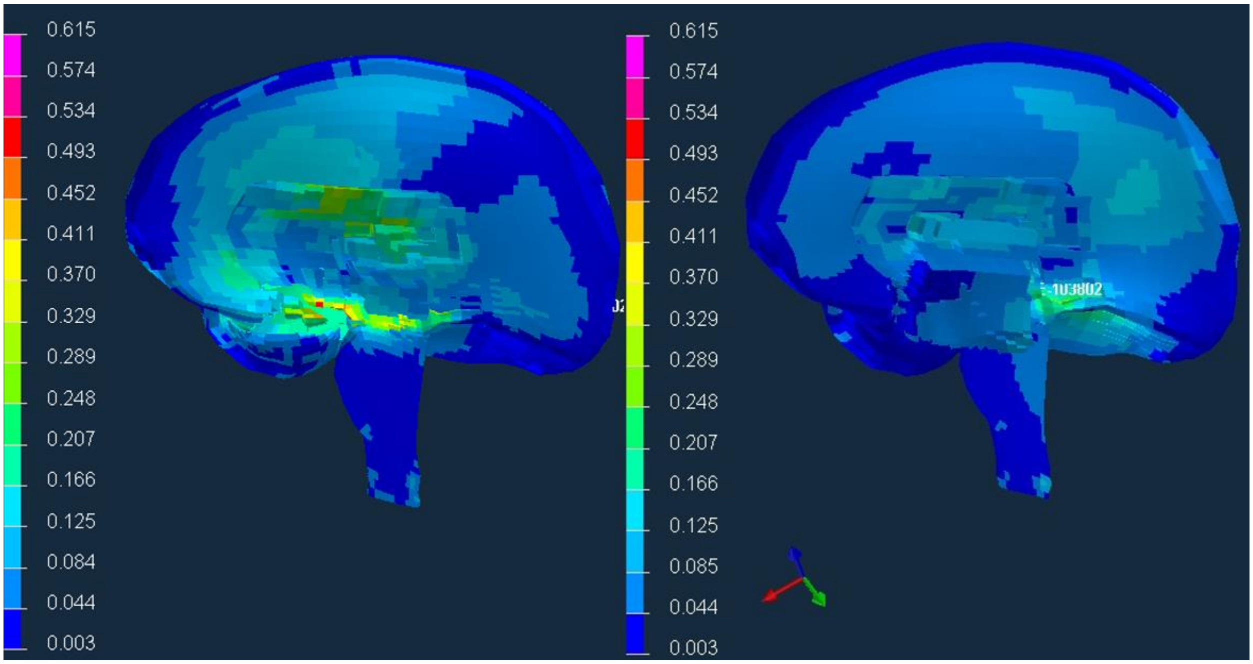

Figure 10. *Sagittal cross section of finite element model. Left) LOC concussion Right) Non-LOC concussion*

Cumulative Strain Damage Measure – 10%								
Type of event	Brain regions	LOC concussion (SD)	Non-LOC concussion (SD)	Effect size Cohen's d	P-Value t-tests	Overall % correct classification	P-value logistic regression	Value representing a 50% risk of LOC
Shoulder collisions	Cerebral cortex	0.35 (0.14)	0.12 (0.14)	1.70	**<0.001**	76.7	**0.004**	0.23
	Cerebral white matter	0.25 (0.18)	0.07 (0.14)	1.16	**0.003**	76.7	**0.021**	0.13
	Corpus callosum	0.32 (0.17)	0.08 (0.11)	1.60	**<0.001**	80.0	**0.006**	0.18
	Thalamus	0.20 (0.16)	0.06 (0.13)	0.93	**0.016**	73.3	**0.039**	0.12
	Brainstem	0.03 (0.03)	0.01 (0.01)	1.12	**0.005**	86.7	**0.022**	0.01
	Brain (whole)	0.28 (0.13)	0.09 (0.12)	1.60	**<0.001**	80.0	**0.005**	0.17
Helmet-to-helmet collisions	Cerebral cortex	0.57 (0.18)	0.46 (0.20)	0.59	0.06	*Logistic regression not statistically significant*		
	Cerebral white matter	0.56 (0.23)	0.40 (0.23)	0.66	**0.036**	62.8	**0.043**	0.47
	Corpus callosum	0.71 (0.24)	0.57 (0.28)	0.53	0.088	*Logistic regression not statistically significant*		
	Thalamus	0.62 (0.27)	0.45 (0.27)	0.66	**0.036**	55.8	**0.042**	0.52
	Brainstem	0.29 (0.22)	0.18 (0.34)	0.38	0.212	*Logistic regression not statistically significant*		
	Brain (whole)	0.54 (0.19)	0.41 (0.20)	0.64	**0.041**	58.1	**0.049**	0.46
Falls	Cerebral cortex	0.48 (0.14)	0.28 (0.22)	1.11	0.117	*Logistic regression not statistically significant ($n_1=n_2=5$)*		
	Cerebral white matter	0.46 (0.18)	0.20 (0.28)	1.12	0.114	*Logistic regression not statistically significant ($n_1=n_2=5$)*		
	Corpus callosum	0.56 (0.16)	0.25 (0.21)	1.70	**0.028**	*Logistic regression not statistically significant ($n_1=n_2=5$)*		
	Thalamus	0.52 (0.14)	0.19 (0.28)	1.50	**0.045**	*Logistic regression not statistically significant ($n_1=n_2=5$)*		
	Brainstem	0.23 (0.12)	0.11 (0.12)	0.97	0.165	*Logistic regression not statistically significant ($n_1=n_2=5$)*		
	Brain (whole)	0.47 (0.15)	0.23 (0.23)	1.32	0.07	*Logistic regression not statistically significant ($n_1=n_2=5$)*		
All events collapsed	Cerebral cortex	0.48 (0.19)	0.31 (0.24)	0.78	**0.001**	61.0	**0.002**	0.40
	Cerebral white matter	0.43 (0.25)	0.26 (0.26)	0.71	**0.002**	62.2	**0.003**	0.34
	Corpus callosum	0.55 (0.27)	0.35 (0.32)	0.66	**0.004**	61.0	**0.006**	0.45
	Thalamus	0.46 (0.30)	0.27 (0.29)	0.62	**0.006**	61	**0.008**	0.36
	Brainstem	0.19 (0.20)	0.11 (0.25)	0.35	0.121	*Logistic regression not statistically significant*		
	Brain (whole)	0.44 (0.20)	0.27 (0.23)	0.77	**0.001**	63.4	**0.002**	0.35

Table 15. *Means of CSDM-10% in the cerebral cortex, cerebral white matter, the corpus callosum, the thalamus and the brainstem, p-value of t-tests and logistic regression results for different types of impact events leading to LOC and non-LOC concussions. The statistically significant results are in* ***bold.***

Strain rate

The t-tests and logistic regressions were statistically significant for all the brain regions for the shoulder and helmet-to-helmet collisions and all the events collapsed with the exception of falls. Table 16 provides the means for strain rate for LOC and non-LOC concussions for the different types of events as well as the p-value for the t-tests and the results of the logistic regressions.

Strain Rate (s^{-1})								
Type of event	Brain regions	LOC concussion (SD)	Non-LOC concussion (SD)	Effect size Cohen's d	P-value t-tests	Overall % correct classification	P-value logistic regression	Value representing a 50% risk of LOC
Shoulder collisions	Cerebral cortex	48 (14)	30 (12)	1.41	**0.001**	83.3	**0.009**	37
	Cerebral white matter	42 (18)	24 (17)	1.02	**0.009**	86.7	**0.028**	31
	Corpus callosum	35 (13)	19 (9)	1.45	**<0.001**	90.0	**0.006**	25
	Thalamus	31 (11)	18 (12)	1.14	**0.004**	80.0	**0.018**	23
	Brainstem	33 (12)	18 (8)	1.45	**<0.001**	83.3	**0.007**	24
Helmet-to-helmet collisions	Cerebral cortex	109 (51)	68 (27)	1.00	**0.002**	74.4	**0.013**	80
	Cerebral white matter	85 (38)	58 (25)	0.82	**0.011**	67.4	**0.026**	69
	Corpus callosum	76 (34)	49 (22)	0.94	**0.004**	76.7	**0.014**	59
	Thalamus	61 (27)	40 (15)	0.91	**0.005**	67.4	**0.016**	48
	Brainstem	72 (27)	45 (17)	1.10	**0.001**	67.4	**0.005**	55
Falls	Cerebral cortex	89 (33)	54 (37)	1.01	0.149	*Logistic regression not statistically significant (n_1=n_2=5)*		
	Cerebral white matter	96 (46)	45 (26)	1.38	0.06	*Logistic regression not statistically significant (n_1=n_2=5)*		
	Corpus callosum	68 (25)	38 (27)	1.19	0.097	*Logistic regression not statistically significant (n_1=n_2=5)*		
	Thalamus	57 (18)	32 (17)	1.43	0.054	*Logistic regression not statistically significant (n_1=n_2=5)*		
	Brainstem	54 (13)	42 (27)	0.55	0.403	*Logistic regression not statistically significant (n_1=n_2=5)*		
All events collapsed	Cerebral cortex	85 (48)	52 (29)	0.81	**<0.001**	62.2	**0.002**	64
	Cerebral white matter	70 (39)	44 (27)	0.78	**0.001**	67.1	**0.002**	56
	Corpus callosum	60 (33)	37 (23)	0.82	**<0.001**	58.8	**0.002**	47
	Thalamus	50 (25)	31 (17)	0.84	**<0.001**	61	**0.001**	39
	Brainstem	55 (28)	35 (20)	0.83	**0.001**	67.1	**0.001**	44

Table 16. *Means of Strain rate in the cerebral cortex, cerebral white matter, the corpus callosum, the thalamus and the brainstem, p-value of t-tests and logistic regression results for different types of impact events leading to LOC and non-LOC concussions. The statistically significant results are in* ***bold.***

Discussion

This study found that concussions with a loss of consciousness occur in association with greater magnitudes of impact velocity, peak linear and peak rotational accelerations than concussions without loss of consciousness and resulted in greater brain tissue deformation in all the brain regions analysed. On average, the cases of concussions with LOC had a maximum principal strain 10% higher than the cases of concussions without LOC. Depending upon the type of event leading to the injury, the volume of the brain experiencing a strain greater than ten percent was 1.3-3.1 times higher in the LOC group. Strain rate is on average 1.5 to 2.1 times greater in the LOC group than the concussion without LOC group. Although this study was not designed to determine whether greater brain tissue deformation to the deep structures of the brain is the cause of LOC in concussive head impacts, the results demonstrate that these structures sustained greater trauma, supporting the notion that LOC is a more severe injury than non-LOC concussions. Therefore, it might be appropriate to reassess the need for delaying a return to contact sports in athletes who have sustained a loss of consciousness.

The predictive capacity of the kinematic data was dependent upon the type of event leading to LOC. Linear acceleration accurately predicted LOC in 70% of cases for shoulder collisions and 83.3 % of cases of helmet-to-helmet collisions. Rotational acceleration was predictive at 83.3 and 69% for shoulder and helmet-to-helmet collisions respectively. The predictive value of peak accelerations decreased when the event types were collapsed for analysis. Impact velocity became the best predictive variable with 80.5 % accuracy. Other variables, including the brain tissue deformation in each brain region have predictive capability lower than 70%, when the events are collapsed. This demonstrates that LOC can be caused by more than one mechanism of energy transfer to the brain, but high energy, reflected in this study by high impact velocity, is the most significant factor in the production of LOC in American football. High energy impacts have been linked to greater brain trauma to deeper structures of the brain (Lighthall, 1988; Yan, et al., 2013) increasing the risk for severe head injuries. In American football, the wide receivers are more at risk to sustain high velocities impact due to the nature of their position. Typically, these athletes have the time and space to reach higher running speed. The defensive players chasing them need to reach similar speed to catch them and tackle them resulting in high velocity collisions. This aspect of the game is reflected in the distribution of players sustaining a concussion with a loss of consciousness. In this study, 46% of concussion cases with LOC were sustained by wide receivers [Appendix B5]. This finding support the notion that the risk of LOC could be managed by enforcing rules aiming at decreasing the velocity of impact and protecting the wide receivers.

The values of peak linear and rotational acceleration reported in this study are consistent with previous studies investigating concussive injuries in professional American football. Viano (2005) reported peak linear acceleration ranging from 59 to 138 g and peak rotational acceleration ranging from 3476 to 9590 rad/s^2 for helmet-to-helmet collisions. Their averages were closer to the LOC concussions in this study and this is likely a reflection of their calculated impact velocity being in the same range as the velocity obtained for the LOC group. They used the size of the helmet as calibration which could have overestimated the impact velocities. The same method was used in this study but only for the fall injuries due to the lack of vertical landmark in proximity to the impacts. This is a limitations of the velocity calculations for fall impacts. The peak linear and rotational acceleration for the fall impacts were smaller than those reported in the literature for helmet-to-helmet injuries. As stated earlier, the magnitudes of peak linear and rotational acceleration are influenced by the type of injury event, with fall and shoulder injuries having more compliance decreasing peak accelerations and increasing duration.

The values of MPS associated with a 50% risk of concussion in the literature range from 0.15-0.32 (Patton, et al, 2013; Kleiven, 2007; McAllister et al., 2012; Kimpara and Iwamoto, 2012). The values for the non-LOC concussion group mostly fall within this range with the exception of the helmet-to-helmet collisions in the cerebral cortex and cerebral white matter, and the cerebral cortex with all the events collapsed. However, they are consistent with Pellman (2003) who reported averages between 0.10 and 0.45 for helmet-to-helmets concussions. The MPS for the LOC concussion group was either within the range or above it. This is not surprising considering the concussion cases with LOC have greater brain tissue deformation than non-LOC concussions. Values of 0.18 and 0.60 for CSDM-10 in the whole brain have been reported in the literature to represent a 50% risk of concussion (Kleiven, 2007; Kimpara, 2012). All the values of CSDM-10 reported in this study are within this range with the exception of the shoulder impacts. This is likely a result of the energy attenuating capability of the compliant shoulder. Viano et al. (2005) reported average strain rates between 34.5 and 81.5 s^{-1} in a set of helmet-to-helmet concussive impacts in American football including both LOC and non-LOC cases. This is consistent with the strain rates observed in the helmet-to-helmet collisions obtained in this study. The strain rates for the falls, the shoulder LOC cases and with all the events collapsed are also within this range. Again, the strain rates associated with the non-LOC shoulder impacts are lower. Despite the shoulder collisions consistently having lower values of brain tissue deformation, this type of impact to the head is capable of injuring an athlete including loss of consciousness. This suggests that the mechanism of injury associated with shoulder impacts may have a component other than pure magnitude, such as duration of exposure of the load on the brain.

Limitations

Limitations to this study include the hybrid III headform is not a fully biofidelic representation of a 50th percentile male and may not represent all the athletes included in this study. The reconstruction process involve the analysis of a two-dimensional video to replicate the three dimensional conditions in which the injury has occur. This may lead to some error in perception and may not accurately reflect the injury conditions. The Wayne State University Brain Injury Model also present some limitations. The WSUBIM is a linear viscoelastic model which leads to increase strain with longer duration of acceleration (Zhang, Yang, & King, 2001). Newer finite element model of the brain use a hyperelastic model to account for the differences in stiffness and non-linearity on tension and compression. Unfortunately, this type of model was not available for this research. Moreover, the brain motion was only validated using one localized brain motion cases and the correlations were poor. This model's validation was focused on skull fracture and intracranial pressure which can make conclusion on brain tissue deformation challenging. In addition, the WSUBIM model was not validated for all the brain regions used in this study. These limitations may alter the values of the variables measured in this study but were constant for both injury group. It is therefore unlikely that it affected the results of the comparisons.

Linear acceleration was found to be a good predictor of LOC in helmet-to-helmet collisions. This is may reflect the reconstruction methods for these type of events that result in high magnitudes for linear acceleration. Linear acceleration is secondary in creating brain tissue deformation due to the incompressible nature of the brain and less likely to result in loss of consciousness.

The values of brain tissue deformation vary with the sports investigated, the type of injurious event, the finite element model used, the brain regions analyzed, and the laboratory reconstruction set-up. In addition, values representing a 50% risk of injury are greatly influenced by the characteristic of the control group. These factors are responsible for the wide range of suggested thresholds in the literature. This represent a challenge in the field of head impact biomechanics because values obtained using different systems cannot be directly compared to one another. However, finite element models can help answer questions pertaining to severity of injury when the study design takes into account their limitations.

None of the logistic regression performed for the falls were statistically significant due to out small sample size (n=5 in each group). However, in American football, concussions from fall only represent a small proportion (11%) of concussive injuries (Pellman, 2003; part 3). Therefore, it was difficult to find cases of concussion with a loss of consciousness for this type of event.

Conclusion

The presence of loss of consciousness from a head impact reflects a greater magnitude of brain tissue trauma. This suggests that concussion with a loss of consciousness are more severe and may require a different return to play protocol. Impact velocity was the most significant predictor of LOC in elite American football and is responsible for greater brain tissue deformation in deep structures of the brain. Wide receivers represented almost 50% of the players who had lost consciousness are particularly at risk for high energy impacts. Rules designed to mitigate this aspect of the game would decrease the risk of a loss of consciousness in American football.

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Study Three

Abnormal motor response associated with concussive injuries: biomechanical comparison between impact seizures and loss of consciousness

Abstract

Context: Loss of consciousness and impact seizures associated with concussion represent a different clinical presentation of concussion however they are often investigated or treated similarly. The biomechanical parameters differentiating between these two distinct signs of injury are poorly described.

Objective: To differentiate between cases of concussions with loss of consciousness and cases with impact seizures by comparing the impact velocity, peak linear and peak rotational acceleration as well as brain tissue deformation in the cerebral cortex, white matter, brainstem, cerebellum, thalamus and corpus callosum.

Design: Descriptive laboratory study

Patients or Other Participants: Elite American football players who sustained a loss of consciousness (20) or impact seizures (21).

Main Outcome Measure(s): Impact velocity, peak linear and peak rotational acceleration, maximum principal strain (MPS), cumulative strain damage measure at 10 % (CSDM10), and strain rate

Results: Strain rate in the cerebral white matter was significantly greater in the LOC group than the impact seizure group. Similar trends were also observed with strain rates in the cerebral cortex, the brainstem and the corpus callosum. There was no statistically significant differences between groups for the other variables in this study.

Conclusions: Lower strain rate in certain brain regions help explain why motor functions is preserved and can be observed in cases of impact seizures when compared to cases of LOC in concussive injuries.

Key Words: Loss of consciousness, impact seizure, strain rate, American football

Introduction

On rare occasions impact seizures are an abnormal motor response observed following concussive impacts. The clinical signs include flexor behavior, extensor behavior or a combination of both in the upper and/or lower extremities.[1-3] The few researchers that have investigated impact seizures in sport-related concussions, have used different terms to describe them.

McCrory et al.[1,4] retrospectively evaluated videos from Australian football and rugby league videos of concussive impacts and described 22 cases of abnormal motor response as concussive convulsions. They characterized six cases as an initial tonic posture, and 20 of their cases with myoclonic jerks. They described seventeen cases as being bilateral, while seven cases demonstrated some lateralizing features. All athletes had normal imaging and all returned to play within two weeks of the injury.

McCrory and his coworkers followed this research by prospectively investigating acute motor and convulsive manifestations in sport-related events.[5] In this study, they observed 102 cases of concussions with convulsive and/or motor features and classified as: loss of consciousness (LOC) (n=75), tonic posturing (n=25), clonic movements (n=6), unsteady gait (n=42), and righting movement (n=40). Again, none of the athletes displayed abnormalities on neuroimaging and all returned to play without any sequelae.

Hosseini and Liftshitz[2] screened videos for the presence of loss of consciousness and reported that 66% of concussions with loss of consciousness present with a form of abnormal motor response that they defined as the fencing response. The authors then attempted to replicate similar responses in rats using fluid percussion injury. They found that the fencing response could only be elicited with an impact consistent with moderate severity of injury but not with a mild severity impact or sham impact. The authors then postulated that cases of head impacts with a fencing response were more severe than those without. Studies using rodents and fluid percussion model may not translate well to sports concussions in human subjects. However, Hosseini and Liftshitz's work is unique as it is the only study that attempts to characterize the magnitudes of impact that lead to impact seizures in concussive injuries. To the authors' knowledge, no study have evaluated the magnitudes of impact in human subjects.

The current literature on impact seizures suggest it is closely related to loss of consciousness and the National Football League has recently announced that cases of impact seizures would be treated the same as a loss of consciousness in their concussion protocol. Impact seizures and LOC seem to be closely related as they often occur concomitantly, however, they do represent a different clinical manifestation of concussive injuries. In impact seizures, a motor response is still present whereas a loss of consciousness is characterized by a complete loss of motor tone. This difference could possibly be explained by the biomechanics of the concussive events and the resulting brain tissue deformation.

Adams and Victor[6] suggested that a sign or a symptom of a brain injury is an expression of both the brain regions that are dysfunctional and those that are normally or overly activated. The authors expected that cases presenting with impact seizures are the result of lower brain tissue deformation in specific brain regions to allow for some motor function to be preserved when compared to cases of loss of consciousness.

Researchers have proposed that both LOC and impact seizures associated with head injuries are caused by dysfunction in the deep structures of the brain, such as the thalamus, the brainstem and the cerebellum.[3,7-11] The depth of brain tissue deformation is related to impact energy, and impact velocity.[12-13]

Physical reconstruction and finite element (FE) modeling of head impact are tools to estimate brain tissue deformations associated with these impacts and understand the biomechanics of the impact that lead to them. Researchers have used physical reconstruction of head impacts in sports to differentiate between concussion and no injury impacts in the past.[14-16] Previous studies have examined the relationship between maximum principal strain (MPS), cumulative strain damage at 10% (CSDM10) and strain rate (SR) and concussions, and have reported these metrics associated with these types of injuries.[16-19] Thresholds for a 50% risk of concussions range from 0.19-0.27 for maximum principal strain, from 0.35-0.47 for CSDM10%, and from 48.5- 57.4s^{-1} for strain rate.[16-19] These values varied depending on the type of impacts being reconstructed, the model being used and the region of the brain measured. Scientists have also used peak linear and peak rotational acceleration from laboratory reconstructions to differentiate between cases of concussions and no-injury head impacts.[15,16] Zhang et al.[16] reported a 50% risk of concussion in American football of 82 g and 5900 rad/s^2 for peak linear and rotational acceleration respectively. Viano and Casson[15] reported average peak linear acceleration of 94g and average peak rotational acceleration of 6432 rad/s^2.

In American football, LOC occurs in approximately eight percent of reported concussion cases.[20] The incidence of impact seizures in American football has not been studied nor has the biomechanical differences between these two clinical signs of concussion been defined. A better understanding of the biomechanics associated with loss of consciousness and impact seizures could provide information about the severity of the impacts that cause them. The purpose of this study was to differentiate between cases of concussions with loss of consciousness and cases with impact seizures by comparing the impact velocity, peak linear and peak rotational acceleration, and brain tissue deformation (MPS, CSDM10, and SR).

Methods

Cases selection

The authors reviewed five years of video footage (1280 games) and press releases from elite American football games to identify cases of concussions with abnormal motor responses; concussions with loss of consciousness or concussions with impact seizures. We included cases for which the medical team had issued a press release confirming the diagnosis of concussion.

The authors divided the cases into an impact seizure group or a LOC group using video evidence of the impact and the period immediately following the impact (0-2 sec). The impact seizure group consisted of athletes that displayed either flexion or extension behavior of the upper and/or lower extremity in any combination. The LOC group consisted of athletes who demonstrated a complete loss of motor tone and the inability to protect themselves following the impact. Cases for which the injury status could not be confirmed were not included in this study.

In total, we included 20 cases of LOC, and 21 cases with impact seizures [See Appendix B4 for a summary of the cases included in this study]. Table 17 displays the number of cases for each type of injury event. We performed a power analysis on pilot data to determine that 16 cases would be sufficient to observe differences in impact velocity, peak linear and rotational accelerations and maximum principal strain in the brain regions included for analysis in this study. However, for the cumulative strain damage measure at 10% and strain rate, the suggested sample size varied between 24 and 523 in each group depending on the brain region. The low incidence of impact seizures in American football and the strictness of the inclusion/exclusion criteria of this study did not allow for the inclusion of such a high number of cases in our analysis. However, this data was reported and the trends interpreted in consideration of the statistical power.

Injury status	**n falls**	**n helmet-to-helmet**	**n shoulder-to-helmet**	**Total**
Impact seizures	2	10	9	21
LOC	3	11	6	20

Table 17. *Number of LOC and impact seizures cases caused by falls, helmet-to-helmet and shoulder collisions. .*

Video analysis for injury reconstructions

The authors performed a video analysis to obtain the impact velocity, the impact location and direction, and the type of event leading to the injury (helmet-to-helmet collision, shoulder-to-helmet collision, or fall). We calculated the impact velocity using Kinovea (0.8.20) [Appendix B2] by determining the distance between the injured player's head and the impacting surface using a calibration grid placed on the field a set time prior to the impact (0.04-0.20 seconds). We set the time prior to impact when we determined that there were no observable changes in velocity from the player prior to the impact (i.e. not being slowed down by a tackle elsewhere on their body, or not being slowed down in a fall by protecting themselves with their arms). To measure velocity using this method, we had to be able to observe the head of the injured player at the time of the impact and at the required time frame for distance measurement. We also had to observe known markers in the frame and on the field to apply a calibration grid and measure the distance prior to the impact. A calibration grid had to be placed on the playing surface in proximity and in the general orientation of the impact. These methods yield measurements errors of less than 10% in ice hockey.[21] Given that the error is vastly influenced by the size and proximity of the calibration grid, the error is likely to be similar or smaller in American football since there are more markings on the field to establish an optimal calibration grid.

Impact reconstructions

We collected the three-dimensional linear and rotational acceleration using a hybrid III headform with a 3-2-2-2 array of accelerometers[23] mounted on an unbiased neck that allowed similar movement in all planes of motion.[24] Several anthropomorphic test devices exist for head impact testing, with both benefits and disadvantages. The authors chose to perform the reconstruction using the hybrid III because it is the most widely used human impact test surrogate. Also, the unbiased neck used in this study was designed to mimic the hybrid III headform without the directional bias, and a better fit with the hybrid III headform.

We reconstructed injuries caused by falls using a monorail drop rig consisting of a drop carriage attached to a 4.7 m long rail. A pneumatic piston releases the carriage once it has reached the height necessary to obtain the desired impact velocity. A photoelectric time gate placed within 0.02 m of the impact measures impact velocity. The ground was represented by a sample of artificial turf (ACT Global sports turf, Austin, Texas, USA) that included the layers and materials that are common in artificial American football field.

We performed reconstructions of helmet-to-helmet and shoulder-to-helmet collisions using a pneumatic linear impactor consisting of an impacting arm, a sliding table and a frame. For helmet-to-helmet collisions, the impacting arm mass was 15.9 kg and equipped with a hybrid III headform wearing an American football helmet for a total striking mass of 24.0 kg. We used an impacting arm of mass 13.1 kg with a 0.142 m thick VN 602 foam and an American football shoulder pad[22] to reconstruct the shoulder-to-helmet impacts. A photoelectric time gate placed within 0.02 m of the impact measured impact velocity. Figure 11 displays the reconstruction set-ups for each type of events.

Figure 11. *Reconstruction set-ups A) Falls B) Helmet-to-helmet collisions C) Shoulder-to-helmet collision.*

We used video analysis to determine the type of helmets the injured players were wearing and used helmets with the same type of liners for our reconstructions. We did not impact helmets at the same location for more than one case (three trials) for the purpose of consistency.

Finite element modeling

We used the Wayne State University Brain Injury Model (WSUBIM) to obtain maximum principal strain, cumulative strain damage above 10%, and strain rate in the cerebral cortex, the cerebral white matter, the corpus callosum, the thalamus, the brainstem, and the cerebellum (Figure 12). We used PAM-CRASH (ESI, Farmington Hills, MI, USA) to run the simulations. The material properties and the model validation can be found in Zhang et al.[25] The authors chose the WSUBIM because, of the models available to them, it possesses the most stable brainstem even though this region is not validated in any finite element brain model.

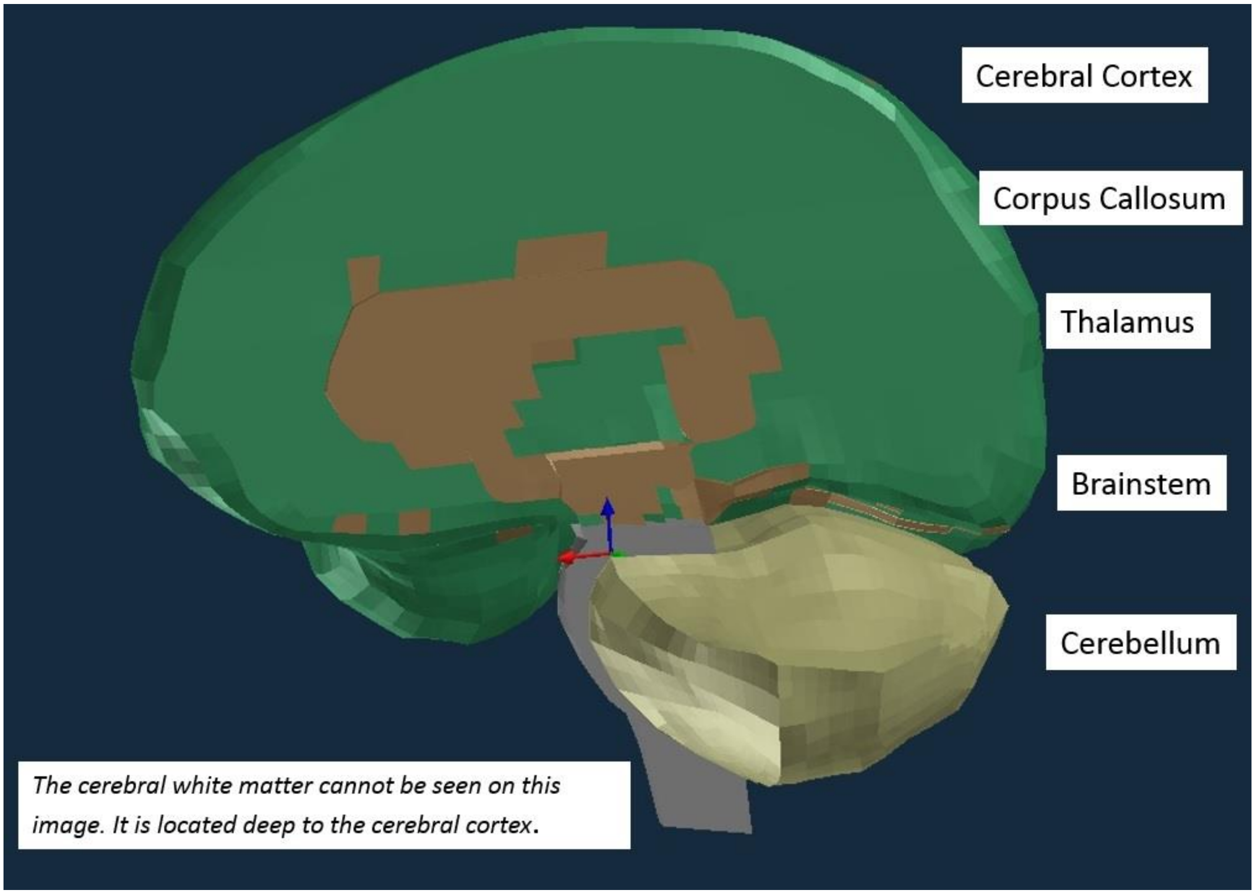

Figure 12. *Wayne State University Brain Injury Model and regions of interests (PAM- CRASH, ESI, Farmington Hills, MI, USA).*

Statistical analysis

We performed independent sample t-tests to investigate the differences between cases of LOC and cases of LOC with impact seizures for peak linear acceleration, peak rotational acceleration, impact velocity, as well as MPS, CSDM10, and strain rate in the cerebral cortex, corpus callosum, the remainder of the cerebral white matter, the thalamus, the brainstem and the cerebellum. The remainder of the cerebral white matter is defined as the white matter identified by the WSUBIM without the portion corresponding to the corpus callosum. The alpha level was set to 0.05. The effect size was calculated using Cohen's D.

Results

The kinematic data are reported in Table 18, average brain tissue deformation (MPS, CSDM10, and strain rate) are reported in Tables 18, 20, and 21. We did not find statistical differences between the LOC group when compared to the impact seizures group for any of the variables with the exception of strain rate in the white matter which was significantly higher for the LOC group.

Kinematic Variables	LOC	Impact seizures	Effect Size (Cohen's d)	p-value	Power
Impact velocity (m/s)	8.7±1.6	8.7±1.5	0.02	0.975	0.979
Peak linear acceleration (g)	80.9±39.8	64.2±32.3	0.46	0.150	0.835
Peak rotational acceleration (rad/s^2)	5595±2472	4972±2379	0.25	0.416	0.829

Table 18. *Means and standard deviations of impact velocity, peak linear and peak rotational acceleration for LOC and impact seizures.*

Maximum principal strain					
Brain region	LOC	Impact seizures	Effect Size Cohen's d	p-value	Power
Cerebral cortex	0.59±0.27	0.48±0.15	0.46	0.149	0.898
Cerebral white matter	0.47±0.18	0.39±0.10	0.57	0.077	0.951
Brainstem	0.38±0.16	0.32±0.10	0.34	0.286	0.914
Cerebellum	0.22±0.08	0.20±0.06	0.19	0.542	0.924
Thalamus	0.33±0.15	0.28±0.09	0.40	0.223	0.877
Corpus Callosum	0.38±0.18	0.32±0.10	0.42	0.237	0.862

Table 19. *Means and standard deviations of maximum principal strain in the cerebral cortex, cerebral white matter, brainstem, cerebellum, thalamus and corpus callosum associated with LOC and impact seizures.*

Cumulative Strain Damage Measure- 10%					
Brain region	LOC	Impact seizures	Effect size Cohen's d	p-value	Power
Cerebral cortex	0.49±0.19	0.47±0.19	0.11	0.733	0.857
Cerebral white matter	0.45±0.26	0.42±0.23	0.11	0.720	0.569
Brainstem	0.21±0.21	0.17±0.20	0.15	0.628	0.050
Cerebellum	0.26±0.23	0.19±0.20	0.32	0.308	0.126
Thalamus	0.48±0.33	0.43±0.27	0.16	0.621	0.386
Corpus callosum	0.55±0.30	0.55±0.24	0.06	0.985	0.605
Full brain	0.45±0.22	0.42±0.18	0.15	0.641	0.746

Table 20. *Means and standard deviations of cumulative strain damage at 10% in the cerebral cortex, cerebral white matter, brainstem, cerebellum, thalamus and corpus callosum associated with LOC and impact seizures.*

Strain rate (s^{-1})					
Brain region	LOC	Impact seizures	Effect size Cohen's d	p-value	Power
Cerebral cortex	98.5±58.9	70.5±30.5	0.59	0.068	0.764
Cerebral white matter	**83.7±47.7**	**57.8±23.4**	**0.69**	**0.037***	**0.842**
Brainstem	60.8±32.7	49.7±21.5	0.40	0.205	0.769
Cerebellum	46.7±22.8	42.4±17.8	0.21	0.503	0.770
Thalamus	55.4±30.4	53.8±18.0	0.46	0.144	0.647
Corpus Callosum	67.9±40.3	51.9±21.3	0.49	0.118	0.729

Table 21. *Means and standard deviations of strain rate in the cerebral cortex, cerebral white matter, brainstem, cerebellum, thalamus and corpus callosum associated with LOC and impact seizures.*

Discussion

We hypothesized that the impact seizure group would have lower magnitudes of brain tissue deformation. We found that this hypothesis was true for strain rate and statistically significant in the white matter (effect size = 0.69). The cerebral cortex, the brainstem, and the corpus callosum showed a similar trend for which impact seizures had lower strain rates but it did not reach statistical significance. However, the observed statistical power was insufficient (<0.80) to dismiss the possibility that strain rate in these regions could be significantly greater in the LOC group if the authors could have included a larger number of cases. Several researchers have described strain rate as being an important measure of neuronal dysfunction and neuronal cell death.[26-29] This supports the notion that impact seizure may be the manifestation of some function being preserved in some brain regions or white matter tracts that allow for the activation of certain muscle groups. Impact seizures were associated with a significantly lower rotational acceleration around the x-axis (p=0.039), explaining the lower strain rates. This difference is likely to be the result of differences in impact location between the two groups. The sample size did not allow for statistical analysis to determine a difference for impact location but the LOC group seems to be associated with two clusters of impact sites, one that is located on the side and centric in nature, and another that is non-centric in nature. In contrast, impact locations associated with impact seizures are sparser (Figure 13).

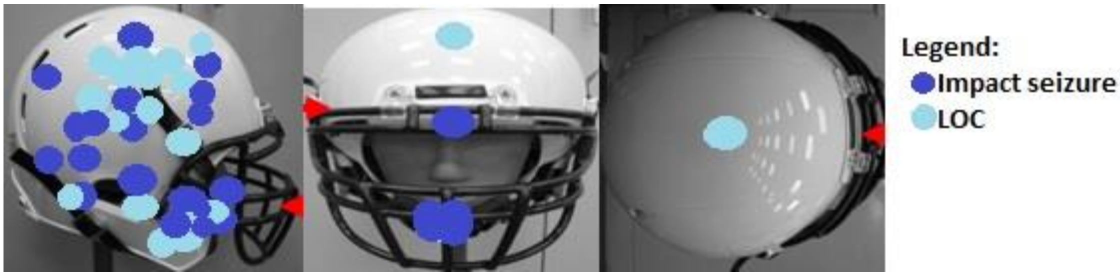

Figure 13. *Impact locations associated with impact seizures and loss of consciousness.*

There was no statistical differences for any brain regions between the two groups for MPS and CSDM10. Despite the low power associated with CSDM10, the differences between the two groups are minimal and may not be clinically relevant. The power was sufficient to conclude that there is no difference in MPS for any brain regions between LOC and impact seizures. The LOC and impact seizure group were homogenous in terms of impact velocity, and types of events that lead to the injury. It is possible that we did not detect differences in magnitudes and volume of strain between the two groups because MPS and CSDM10 are less sensitive to the interactions of the factors that characterize the impacts (impact velocity, impact location/direction, compliance and striking mass) when the two groups are so similar. The magnitudes of strain reported in the present study are greater than what researchers using similar methods have described in both our injury groups. This suggest that LOC and/or impact seizures are more severe than concussions without these signs in terms of magnitude of strain. Kleiven[17] reported MPS of 0.21 to be indicative of a 50% risk of concussion while Patton et al.[18] suggested MPS of 0.15, 0.15 and 0.27 to be indicative of 50% concussion risk in the midbrain, corpus callosum and grey matter respectively. As expected both research teams report mean values below the values obtained in this study in all brain regions.[17,18] Because these researchers used finite element brain models with different brain material properties and comparisons across finite element model should be done carefully. Zhang et al.[16] used the WSUBIM and reported a maximum principal strain of 0.24 to define an 80% risk of concussive injury in American football. All the MPS values reported in this study are above the 80% risk value suggested by Zhang et al.[16] with the exception of the cerebellum. Magnitudes of brain tissue strain are linked to severity of injury, i.e. higher strains associate with greater dysfunction and perhaps tissue death.[27-29] Although this research was not designed to provide information on return-to-play protocols following loss of consciousness and impact seizures associated with concussive impacts, their association with severity of brain trauma suggests that further research is necessary to understand the need to delay the return to contacts sports when these signs are observed in an athlete.

We did not detect any differences in impact velocity, peak linear and peak rotational acceleration between the two groups. Our groups consisted of the three most common types of concussive events in American football: falls, shoulders-to-helmet collisions, and helmet-to-helmet collisions.[30] These events resulted in different shapes of acceleration curves characterized by different peak values and durations of acceleration. The values of peak linear and peak rotational acceleration reported in this study were lower than those previously reported for concussions in American football[15,16] despite resulting in larger brain tissue deformation. This demonstrated that there is an interaction between event types and peak accelerations values, and that peak accelerations thresholds should be specific to the event types to be interpreted meaningfully.

Limitations

Certain limitations are inherent to the methods used in this study. We assigned athletes with confirmed concussions to different groups based on video analysis and not on-site evaluations, due to an inability to access this information. To ensure accuracy in group designation, we were careful to eliminate cases for which the response was ambiguous, but we could have misinterpreted the athlete's responses during the video analysis. Ambiguous cases of LOC consisted of videos for which it was unclear whether the athletes were simply resting on the ground for a period of time or if they were truly unconscious. Cases of impact seizures where athletes displayed a brief motor response (< 1 sec) were discarded to avoid including cases where the motor response was voluntary or the result of inertia of the limbs after the impacts. Cases of impact seizures could have been misinterpreted as LOC if the motor response occurred during the fall that ensued from the collision or if the athlete was positioned in such a way that the motor response could not be seen.

Physical reconstructions and finite element modeling of head impacts does not take into consideration individual anatomical and physiological differences that may influence an individual's tolerance to head impacts and their associated responses. The biofidelity of headforms is sometimes compromised to improve reproducibility of testing. Comparisons of responses between headforms can be difficult. Furthermore, finite element brain models only provide an approximation of the brain tissue deformation sustained during the head impact and have specific limitations. For example, the material properties are established based on *in vivo* and *in vitro* animal model of tissue deformation and the methods used in these studies influence the results. Zhang et al.[25] have validated the WSUBIM for pressure and brain motion using studies performed on cadavers, which may not fully represent what happens in a live athlete. In addition, these validations did not include all the brain regions analyzed in this study such as the brainstem and the cerebellum.[25] Another limitation of finite element model is that they are a gross representation of the brain. Improving the details and axonal arrangement of certain brain regions could result in better distinction between various outcomes of clinical presentation. Despite the limitations associated with finite element models of the brain, they were useful in making comparisons between the groups.

Conclusions

This study identified strain rate in the white matter differentiated between the LOC and impact seizure groups. Other regions such as the cerebral cortex, the brainstem and the corpus callosum also presented with lower strain rates in the impact seizure group when compared to the LOC group. This study also shows that athletes with LOC and impact seizures sustain similar magnitude and volume of strain. This demonstrated that overall concussions with impact seizures are similar to concussions with LOC but are more severe than concussions without these signs.

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PART III

Discussion

The main objective of this thesis was to determine the severity of head impacts associated with loss of consciousness and impact seizures in sports. The first study used laboratory impact representations and finite element modeling to compare the head dynamic response and brain tissue deformation of punches that lead to LOC to punches that do not lead to LOC. Video analysis confirmed anecdotal evidence that hooks to the mandibular angle were the most common type of punch that can induce a loss of consciousness. The head dynamic response and brain tissue deformation associated with this type of punch were significantly greater than the other types of punches. These results can be attributed to the combination of an impact location that can induce high magnitudes of rotational acceleration and a technique that typically result in high impact energy due to greater striking velocities (Stojsih, Boitano, Whilelm, & Bir, 2008).

The second study compared cases of concussions with loss of consciousness to cases of concussions without loss of consciousness using laboratory reconstructions and finite element modeling of American football injuries. This study showed that concussions with a loss of consciousness are associated with greater magnitudes of head accelerations and brain tissue trauma regardless of the type of events that led to the injury. Overall, the best predictor of LOC was impact velocity which implies that LOC is influenced by the amount of energy being transferred to the brain and may be prevented through rules that mitigates this aspect of the game.

The third study further investigated the biomechanics associated with cases of LOC by comparing the head dynamic response and brain tissue deformation between cases of LOC with and without impact seizures. The results demonstrated that cases of LOC with impact seizures were the result of significantly smaller strain rates in the white matter. Similar trends were observed in the cerebral cortex and the corpus callosum but the results of the analysis did not reach significance. This difference in strain rate could explain the remaining motor function associated with impact seizures compared to cases of concussion with LOC without a motor response. The impact locations associated with cases of LOC were grouped into two clusters. The first one was located at the center of gravity on the side. The second was non-centric and located on the side of the face similarly to the impact location associated with knockouts in boxing. The latter is typically associated with greater peaks of rotational accelerations (Walsh, Rousseau, & Hoshizaki, 2011). These impact locations resulted in greater magnitude of rotational acceleration in the coronal plane and likely explain the greater strain rates in the LOC group, despite the lack of differences in impact velocity or peak resultant linear and rotational acceleration.

Implications of the findings

Overall, this thesis demonstrated that head impacts associated with loss of consciousness and impact seizures are characterized by greater magnitudes of head dynamic response and greater brain tissue trauma in all brain regions analyzed in this study, including deep structures such as the brainstem compared to other types of head impacts. This supports the magnitude aspect of the theory proposed by Ommaya and Gennarelli (1974) that concussions with a loss of consciousness were the result of greater magnitude of brain trauma or to trauma to a specific region of the brain, or both. Due to the high energy impact loading condition and the limitations of the finite element model, this thesis was not designed to pinpoint to a specific brain region for which high strains induces LOC. However, the brainstem and other deep structures of the brain sustained higher brain tissue deformation in LOC cases. Therefore, the second part of their theory pertaining to a specific brain region could neither be confirmed nor refuted.

The severity of head impacts associated with loss of consciousness and impact seizures suggests that concussive injuries that occur with these signs are more severe in nature. Therefore, concussion management protocols that ignore these clinical outcomes should be re-evaluated. Further research is needed to confirm these findings in humans.

Sport specific prevention guidelines and prevention strategies can be established with guidance from the results obtained in this thesis. In boxing, hooks to the mandibular angle are associated with higher magnitudes of brain trauma. Coaching strategies should aim at perfecting defensive skills against this type of punch. Levels of competition concerned about magnitudes of brain trauma should consider removing hooks from their competitions and training. In elite American football, cases of concussion with LOC were caused primarily by greater impact velocities, and to impact locations principally located on the side of the head. Therefore, rules aiming at mitigating high velocity impacts and impacts to the blind side [Appendix B9] should be enforced in an effort to prevent LOC.

This thesis also supports the notion that dysfunction associated with concussive injuries may not always represent structural damage caused by the injury. The duration of symptoms and the neuropsychological performance observed in athletes who have lost consciousness does not necessarily reflect the brain trauma sustained. As such, clinicians have to be careful when interpreting the results of clinical tests to characterize the severity of injury.

Limitations of this thesis

Limitations to individual studies were described in PART II in the limitations section of each studies. Here is a summary of the major limitations of this thesis:

- The impact velocity associated with boxing impacts could not be obtained using video analysis. Instead of reconstructing injurious events, impact representations were conducted using parameters from the literature. Therefore, the magnitudes of head dynamic response and brain tissue deformation obtained in this thesis can be considered worst-case scenario impacts since they represent unblocked impact without energy management strategies. However, since the magnitudes associated with LOC punches are greater than non-LOC punches in these high energy impacts, it is likely that similar results could be obtained using real-life impacts.
- The clinical outcomes associated with American football concussive injuries were assessed with the combination of video analysis and press releases from the team's medical staff. It is challenging to determine a loss of consciousness or impact seizures using video analysis. Therefore, strict inclusion and exclusion criteria described in study 2 and 3 were used to minimize this bias. This resulted in nine cases being excluded from this thesis due to lack of video evidence regarding the clinical outcome.
- There is a strong likelihood that individual differences in genetics, mechanical properties of the head, and overall anatomical and/or physiological characteristics have an influence on the risk of loss of consciousness and impact seizures. There is an argument for certain individuals to have an increased vulnerability to loss of consciousness. In fact, four

American football players included in this thesis had multiple concussions with loss of consciousness in their career. The methods used in this thesis cannot account for these variables. However, the objective of this thesis was to establish a general understanding regarding the severity of head impacts associated with loss of consciousness and impact seizures and the methods used were able to demonstrate a distinction.

- The finite element modeling of this thesis also present certain limitations. The WSUBIM has limited validation in brain motion and is not validated for all the brain regions analyzed in this thesis. Furthermore, specific brain regions such as the corpus callosum and thalamus are not modeled using material properties specific to these regions but rather with general grey or white matter approach. However, every brain model available is validated using the same data and is likely to react similarly to the same load.
- Finite element model analyses obtained in this thesis often resulted in unusually high magnitudes that do not reflect the magnitudes experienced in humans. This represent the limitations associated with the use of finite element models in general and especially brain models. The values obtained from these analyses are not meant to be taken literally but represent a relative severity when comparing groups. Therefore, when analyzing brain tissue deformation, it is recommended to design studies in which comparisons between groups can be performed as opposed to simply documenting the magnitudes of brain tissue deformation. The values depends on the models used, the material properties assigned to the different regions of the brain, the contact surfaces, the number of elements and many other assumptions made during the development of the model. As such, readers should exercise caution when considering the numerical strain values reported using finite element models but consider their relationship to other groups.
- Multiple independent t-tests were performed in Studies One, Two and Three. This was done to independently evaluate the capacity of each variable to detect differences between groups and establish their sensitivity. This increases the likelihood of a type I error. However, the results of laboratory reconstructions in terms of dynamic response and brain tissue deformation is a direct reflection of the impact characteristics and varies very little between trials. Therefore in this context, the chances of type I error are minimized.

Recommendation for future research

The findings highlighted in this thesis demonstrates that impact velocity and impact location play a role in the risk for loss of consciousness in both boxing and American football. In professional boxing, these factors were linked to a hook to the side of the head. In elite American football, collisions above eight meter per second were associated with a 50% risk of a loss of consciousness, and the majority of impacts were to the side of the head. This suggests that the mechanisms of injury leading to loss of consciousness is specific to the sport being played. In an effort to decrease the risk for a loss of consciousness or impact seizures, similar research should be undertaken to understand how LOC occurs in other contact sports such as ice hockey, lacrosse, as well as other types of combat sports. Furthermore, this research focused solely on professional levels of boxing and American football. Future research should focus on understanding how LOC occurs in different population such as younger individuals to understand how the risk is influenced by age and level of competition.

Furthermore, given the limitations of the WSUBIM and the unique characteristics of different FE brain models, it would be interesting to conduct similar comparisons using different FE models. The results are likely to demonstrate differences in strain levels between concussion with and without LOC, but as the accuracy and validation of the FE models improve, the vulnerability of different brain regions may be more detectable.

Appendices

Appendix A: List of contributions

Journals

Published

Cournoyer, J, Post A, Rousseau P, and Hoshizaki TB. The ability of American football helmets to manage linear acceleration with repeated high-energy impacts. *Journal of athletic training* 51, no. 3: 258-263. 2016

Cournoyer, J, Hoshizaki, TB. Abnormal motor response associated with concussive injuries: biomechanical comparison between impact seizures and loss of consciousness. In revisions in *Journal of Athletic Training. In press* 2018

Submitted (in order of thesis chapter)

Cournoyer, J, Hoshizaki, TB. Brain trauma associated with punches resulting in loss of consciousness in boxing. Submitted to *Journal of Sports and Health Sciences*. 2018

Cournoyer, J, Hoshizaki, TB. Biomechanical comparison of concussions with and without a loss of consciousness in elite American football. Resubmitted to *Sports biomechanics*. 2018

Conferences

Posters

Cournoyer, J, Hoshizaki, TB. Biomechanical comparison of concussions with and without a loss of consciousness in elite American football. AAN: The sport concussion conference, Indianapolis, IN, USA, July 2018

Cournoyer, J, Hoshizaki, TB. Biomechanical comparison of concussions with and without a loss of consciousness in elite American football. Canadian Society of Biomechanics, Halifax, NS, Canada

Appendix B1: NFL Game Day concussion protocol

Figure 14. *NFL Game day concussion protocol (Ellenbogen, et al., 2018).*

Return to Introduction

Appendix B2: Calculation of velocity using Kinovea

Kinovea (version 0.8.20) is a video analysis software that allows for measurements of distance given that there are known markers on the surface to use as reference points. The impact velocity of a collision is calculated by measuring the distance between two players 5 frames prior to the impact (0.2 second). The impact velocity of a fall is calculated using the distance between the head of the players and the ground 2 frames prior to the impact (0.08 second) for falls.

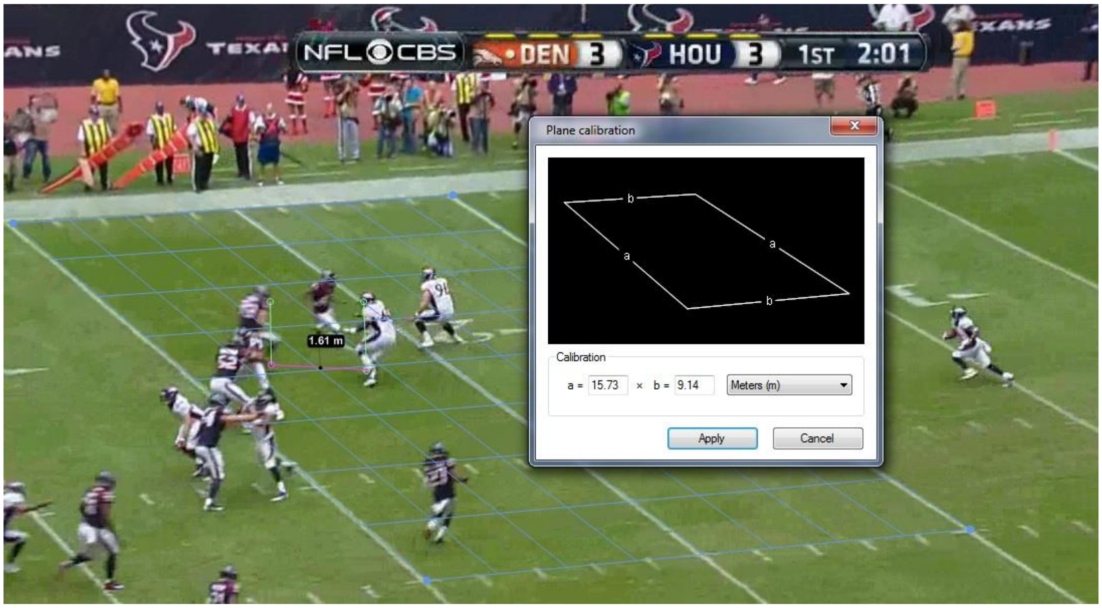

Figure 15. *Example of calculation of velocity for a helmet-to-helmet collision. Distance = 1.61 m, Time = 0.2second. Velocity = 1.61m /0.2 s = 8.05 m/s.*

Measurement error using Kinovea

This method of velocity calculation was validated in ice hockey and the average error associated with this method was approximatively 10% (Post, et al., 2018). The main factors affecting the error are: the size of the calibration, the proximity of the calibration grid, and the orientation of the impact in relation to the camera. In American football, there are more markers on the field of play than in ice hockey and the majority of head impacts occurs in close proximity to these markers. For the cases of head collisions in American football included in this thesis, a calibration grid was placed directly at the site of impact or next to it. In addition, all the cases of collisions included in this study occurred perpendicular to the camera. Therefore, the measurement error associated with the cases included in this thesis is either equivalent or better than that measured in ice hockey. Furthermore, the velocities were calculated twice for each cases and an intra-rater reliability was calculated (ICC=0.96).

Return to Methods Study 2

Return to Methods Study 3

Appendix B3: Impact location grid American football

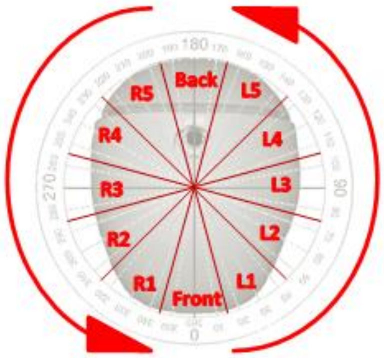

Figure 16. *Impact location reference grid in American football*

Influence of impact location accuracy on dynamic response and brain tissue strain

Quality control of the accuracy of the impact locations was performed by assessing the movement of the head following the impact during the reconstruction process and ensuring it moved similarly to the head of the injured athletes in the videos of the injury. Previous research has shown that minimal changes in impact angles (<10 degrees) does not result in clinically relevant magnitudes of strain (<5%), but that greater differences are created with changes in impacts angles greater than 15 degrees (Oeur & Hoshizaki, 2014). Unpublished data from the NISL by Taylor also suggests that a horizontal displacement of the impact location on the Hybrid III headform equipped with a football helmet has a minimal effect on the magnitude of strain if the difference in location is less than 1.5 inches on side impacts (<7%), or less than one inch on frontal impact locations (<5%) (Figure 18).

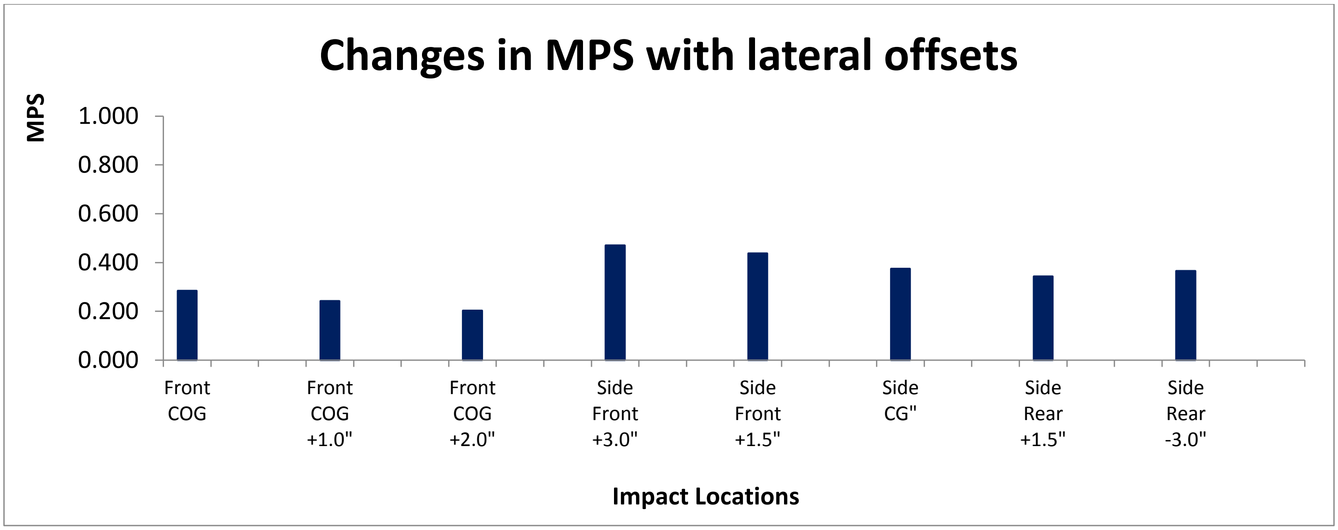

Figure 17. *Changes in magnitude of MPS with lateral offsets on front and side location.*

Appendix B4: Summary of cases of concussions with and without LOC in American Football

Case ID	Player position	Event types	Velocity	Impact location	Helmet Worn	LOC (Y/N)	Motor response
LOC-1	WR	Shoulder	10.9	L1-A	Schutt Air XP Pro	Y	None
LOC-2	RB	Shoulder	7.9	Front-E	VSR4	Y	None
LOC-3	WR	Shoulder	7.7	L1-E	Revolution speed	Y	Bilateral triple flexion upper extremities
LOC-4	DB	Shoulder	10.8	L3-D	VSR4	Y	Bilateral extension elbows and fingers
LOC-5	WR	Shoulder	8.3	L2-F	Schutt DNA pro	Y	Bilateral elbow flexion, fingers extension
LOC-6	DB	Shoulder	8.6	L3-B	VSR4	Y	None
LOC-7	LB	Shoulder	7.9	R2-D	Revolution speed	Y	Right arm fencing
LOC-8	WR	Shoulder	10.1	L4-E	Schutt Air XP Pro	Y	None
LOC-9	WR	Shoulder	7.8	R3-C	VSR4	Y	None
LOC-10	WR	Shoulder	9.2	R1-E	Schutt Air XP Pro	Y	Bilateral triple flexion upper extremities
LOC-11	WR	Shoulder	9.3	R4-C	Schutt Air XP Pro	Y	Bilateral triple flexion upper extremities
LOC-12	LB	Shoulder	9.1	R2-B	Riddell 360	Y	None
LOC-13	TE	Shoulder	9.4	L2-C	Revolution speed	Y	Bilateral triple flexion upper extremities
LOC-14	WR	Shoulder	9.9	L2-B	Riddell 360	Y	Bilateral triple flexion upper extremities
LOC-15	DB	Shoulder	7.9	R4-C	Schutt Air XP Pro	Y	Bilateral triple flexion upper extremities
LOC-16	WR	Helmet	8.5	L5-D	Schutt Air XP Pro	Y	Bilateral triple flexion upper extremities
LOC-17	RB	Helmet	11.4	R1-E	Schutt Air XP Pro	Y	None
LOC-18	WR	Helmet	9.0	L4-B	VSR4	Y	None
LOC-19	WR	Helmet	8.3	R2-E	VSR4	Y	None
LOC-20	DB	Helmet	10.3	R1-D	VSR4	Y	Bilateral triple flexion upper extremities
LOC-22	WR	Helmet	7.8	L4-D	Revolution speed	Y	Bilateral triple flexion upper extremities
LOC-23	RB	Helmet	10.3	L4-E	Revolution speed	Y	Left arm fencing
LOC-24	TE	Helmet	11.4	front-D	VSR4	Y	Left arm triple flexion, right arm fencing
LOC-25	LB	Helmet	8.1	L1-E	VSR4	Y	Bilateral triple flexion upper extremities
LOC-26	WR	Helmet	8.0	L1-E	Schutt Air XP Pro	Y	None
LOC-28	DB	Helmet	8.5	L5-B	Schutt Air XP Pro	Y	Bilateral triple flexion upper extremities
LOC-29	WR	Helmet	8.3	Crown	Schutt Air XP Pro	Y	Left arm triple flexion, right arm fencing
LOC-30	DB	Helmet	9.7	Front -C	VSR4	Y	None
LOC-31	WR	Helmet	9.0	L3-B	Schutt Air XP Pro	Y	None
LOC-32	DB	Helmet	10.9	R3-E	Schutt Air XP Pro	Y	None
LOC-33	DB	Helmet	7.4	L2-F	Revolution speed	Y	None
LOC-34	DB	Helmet	9.5	L4-C	Revolution speed	Y	None
LOC-35	RB	Helmet	8.6	Front-A	Schutt Air XP Pro	Y	None
LOC-36	OL	Helmet	10.2	R2-B	Riddell 360	Y	Bilateral triple flexion upper extremities
LOC-37	QB	Helmet	11.0	R2-C	Schutt DNA Pro	Y	None

LOC-38	RB	Helmet	10.4	L3-A	Revolution speed	Y	Right arm triple flexion, left arm fencing
LOC-39	WR	Fall	5.8	R3-C	VSR4	Y	Bilateral triple flexion upper extremities
LOC-40	QB	Fall	5.0	L3-C	VSR4	Y	None
LOC-41	WR	Fall	4.9	L3-C	VSR4	Y	Right arm triple flexion, left arm elbow flexion
LOC-42	WR	Fall	6.2	R3-B	Revolution speed	Y	None
LOC-43	WR	Fall	7.0	R3-B	Schutt Air XP Pro	Y	None
NoLOC-1	DB	Shoulder	8.2	L4-D	VSR4	N	None
NoLOC-2	RB	Shoulder	7.4	R3-C	Schutt Air XP Pro	N	None
NoLOC-3	LB	Shoulder	5.4	Front-A	VSR4	N	None
NoLOC-4	RB	Shoulder	8.6	R5-B	Riddell 360	N	None
NoLOC-5	RB	Shoulder	7.0	L3-B	Riddell revolution IQ	N	None
NoLOC-6	DB	Shoulder	7.0	L2-D	Schutt Air XP Pro	N	None
NoLOC-7	WR	Shoulder	5.4	R2-E	Schutt Air XP Pro	N	None
NoLOC-8	DL	Shoulder	7.0	Front-A	Revolution speed	N	None
NoLOC-9	DB	Shoulder	8.8	L5-C	Schutt Air XP Pro	N	None
NoLOC-10	LB	Shoulder	6.0	L3-C	VSR4	N	None
NoLOC-11	DB	Shoulder	6.8	L3-D	Schutt Air XP Pro	N	None
NoLOC-12	DB	Shoulder	5.1	R3-C	VSR4	N	None
NoLOC-13	WR	Shoulder	7.5	L2-D	Revolution speed	N	None
NoLOC-14	WR	Shoulder	7.6	R3-B	Riddell 360	N	None
NoLOC-15	RB	Shoulder	6.5	R3-B	Schutt Vengeance	N	None
NoLOC-18	OL	Helmet	7.9	L3-D	Riddell revolution IQ	N	None
NoLOC-19	TE	Helmet	6.9	R3-A	Riddell revolution IQ	N	None
NoLOC-20	TE	Helmet	8.5	R3-A	Riddell revolution IQ	N	None
NoLOC-21	DB	Helmet	8.4	L1-E	Schutt Air XP Pro	N	None
NoLOC-22	RB	Helmet	6.5	L3-C	VSR4	N	None
NoLOC-23	DB	Helmet	7.1	R1-B	Rev Speed	N	None
NoLOC-24	TE	Helmet	6.9	L2-B	Riddell revolution IQ	N	None
NoLOC-25	DB	Helmet	6.8	L4-C	Air XP Pro	N	None
NoLOC-26	TE	Helmet	7.2	R5-D	Revolution speed	N	None
NoLOC-27	OL	Helmet	7.2	R2-R3-E	Riddell revolution IQ	N	None
NoLOC-28	OL	Helmet	7.5	Front-A	Riddell revolution IQ	N	None
NoLOC-29	RB	Helmet	7.2	L1-E	Riddell revolution IQ	N	None
NoLOC-30	DB	Helmet	7.6	R4-A	VSR4	N	None
NoLOC-31	TE	Helmet	6.4	Front B	Revolution speed	N	None
NoLOC-32	LB	Helmet	9.2	R2-D	Revolution speed	N	None
NoLOC-33	OL	Helmet	6.4	L2-B	Revolution speed	N	None
NoLOC-34	DB	Helmet	5.7	R3/R4-D	Xenith X1	N	None
NoLOC-35	OL	Helmet	7.2	Front-A	Revolution speed	N	None
NoLOC-36	DB	Helmet	8.1	Front-C	Riddell 360	N	None
NoLOC-37	RB	Helmet	5.8	L2-E	Riddell 360	N	None

NoLOC-38	QB	Helmet	6.4	L1-F	Schutt Air XP Pro	N	None
NoLOC-39	TE	Fall	4.3	L5-C	Revolution speed	N	None
NoLOC-40	QB	Fall	4.4	R3-C	Schutt DNA Pro	N	None
NoLOC-41	WR	Fall	3.5	Back-D	Schutt DNA Pro	N	None
NoLOC-42	DB	Fall	1.9	L2-C	Riddell revolution IQ	N	None
NoLOC-43	TE	Fall	5.7	L2-D	Revolution speed	N	None

Table 22. *Summary of American football reconstructions used for study 2 and 3.*

The types of abnormal responses detailed in the summary of American football concussion used in study 2 and 3 were evaluated by video analysis to the best of the author's ability. Abnormal motor response is open to being misinterpreted and represents a limitation of using video analysis for inclusion criteria.

Return to Methods Study 2

Return to Methods Study 3

Appendix B5: Distributions of cases by player position for cases of concussion with and without LOC

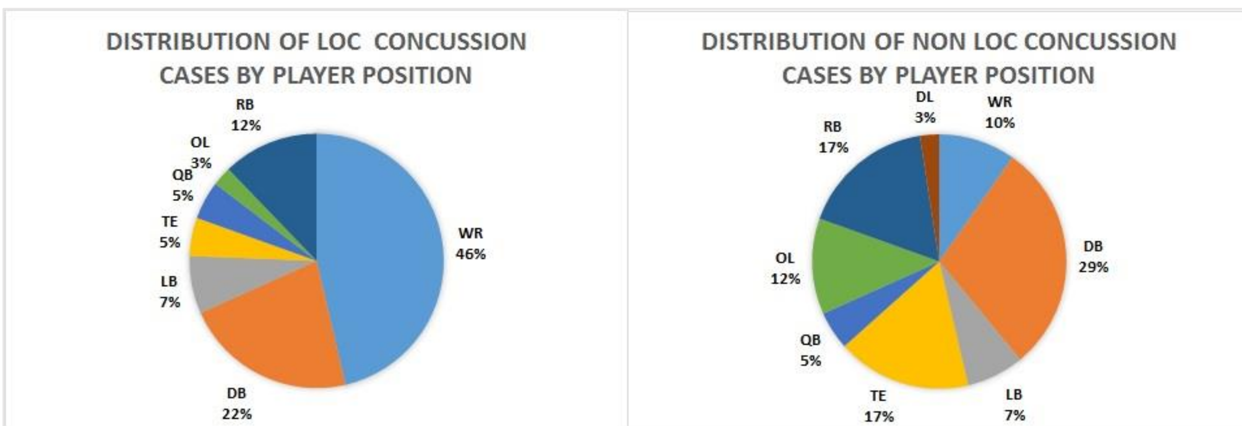

Figure 18. *Distribution of cases of LOC and non LOC concussions by player position. WR= Wide receiver, DB= Defensive back, LB= Linebacker, TE= Tight end, QB= Quarterback, OL= Offensive lineman, DL= Defensive lineman, RB= Running back.*

Return to discussion Study 2.

Appendix B6: Distribution of cases by player position in the NFL

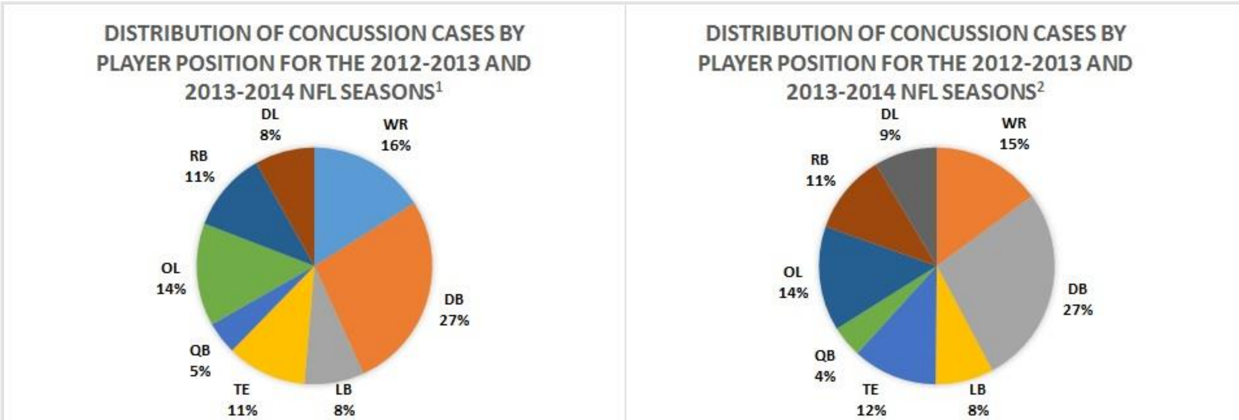

Figure 19. *Distribution of concussion cases by player position. [1.] (Nathanson, et al., 2016) [2.] (Lawrence, Hutchison, & Comper, 2015) WR= Wide receiver, DB= Defensive back, LB= Linebacker, TE= Tight end, QB= Quarterback, OL= Offensive lineman, DL= Defensive lineman, RB= Running back.*

Appendix B7: Distribution of LOC and Non-LOC concussion cases per event type

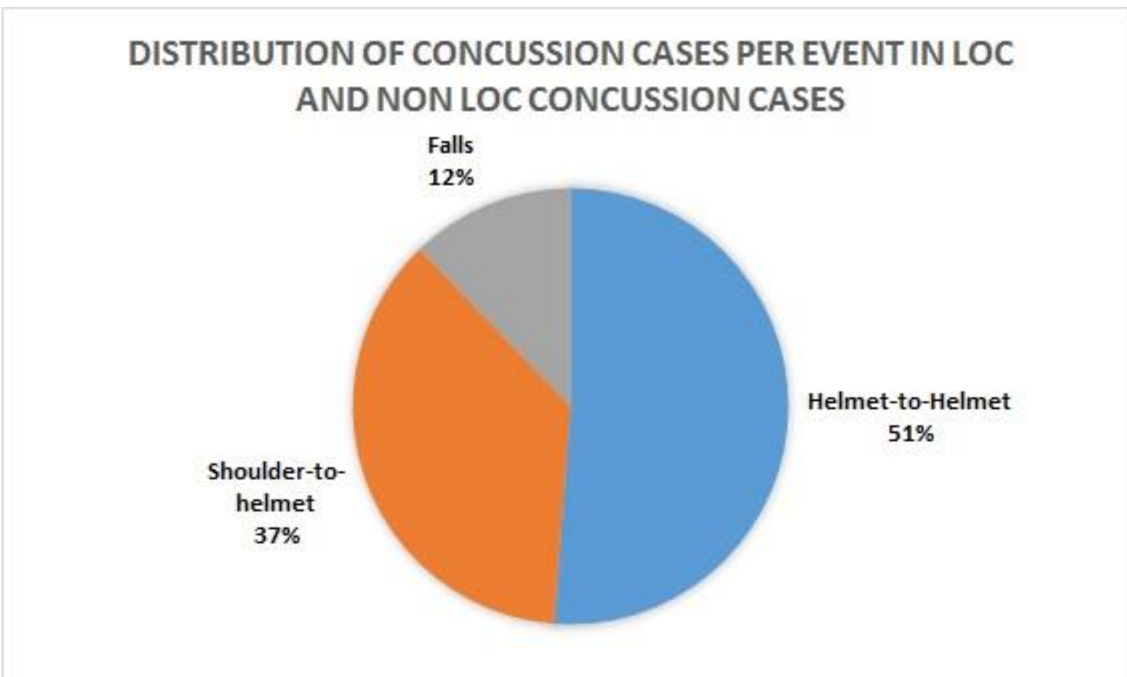

Figure 20. *Distribution of concussions cases with and without LOC by types of injurious event.*

Appendix B8: Distribution of concussion cases per event types in the NFL.

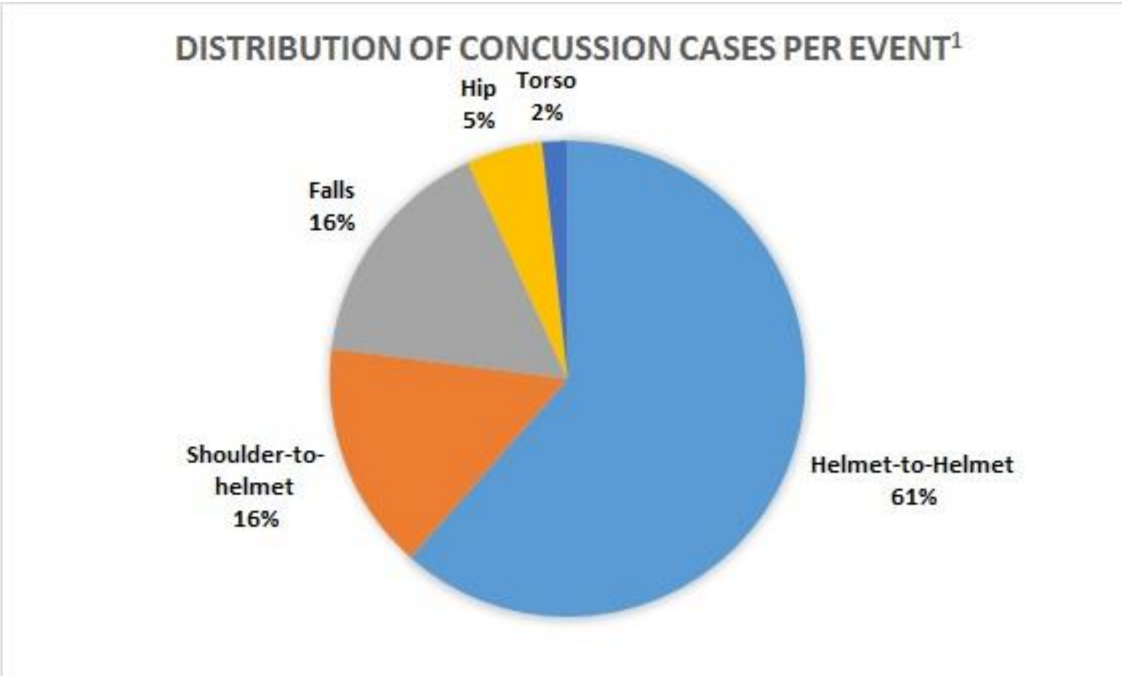

Figure 21. *Distribution of concussions cases by types of injurious events in the NFL. [1.] (Pellman, Viano, Tucker, & Casson, 2003)*

Appendix B9: Current NFL rules to enforce to decrease the risk for LOC in elite American football

*** From the Official 2018 NFL Rulebook https://operations.nfl.com/media/3277/2018-nfl-rulebook_final-version.pdf ***

SECTION2. ARTICLE 7. PLAYERS IN A DEFENSELESS POSTURE. It is a foul if a player initiates unnecessary contact against a player who is in a defenseless posture.

(a) Players in a defenseless posture are:

(1) A player in the act of or just after throwing a pass (passing posture).

(2) A receiver running a pass route when the defender approaches from the side or behind. If the receiver becomes a blocker or assumes a blocking posture, he is no longer a defenseless player.

(3) **A receiver attempting to catch a pass who has not had time to clearly become a runner. If the player is capable of avoiding or warding off the impending contact of an opponent, he is no longer a defenseless player**.

(4) **The intended receiver of a pass in the action during and immediately following an interception or potential interception. If the player is capable of avoiding or warding off the impending contact of an opponent, he is no longer a defenseless player.**

Note: *Violations of this provision will be enforced after the interception, and the intercepting team will maintain possession.*

(5) A runner already in the grasp of a tackler and whose forward progress has been stopped.

(6) A kickoff or punt returner attempting to field a kick in the air.
(7) A player on the ground.
(8) A kicker/punter during the kick or during the return (Also see Article 6-h) for additional restrictions against a kicker/punter).
(9) A quarterback at any time after a change of possession (Also see Article 9-f) for additional restrictions against a quarterback after a change of possession).
(10) A player who receives a "blindside" block when the path of the blocker is toward or parallel to his own end line.
(11) A player who is protected from an illegal crackback block (see Article 2).
(12) The offensive player who attempts a snap during a Field Goal attempt or a Try Kick.

(b) Prohibited contact against a player who is in a defenseless posture is:

(1) forcibly hitting the defenseless player's head or neck area with the helmet, facemask, forearm, or shoulder, even if the initial contact is lower than the player's neck, and regardless of whether the defensive player also uses his arms to tackle the defenseless player by encircling or grasping him;
(2) lowering the head and making forcible contact with any part of the helmet against any part of the defenseless player's body; or
(3) illegally launching into a defenseless opponent. It is an illegal launch if a player (i) leaves both feet prior to contact to spring forward and upward into his opponent, and (ii) uses any part of his helmet to initiate forcible contact against any part of his opponent's body. (This does not apply to contact against a runner, unless the runner is still considered to be a defenseless player, as defined in Article 7.)

Notes:
(1) The provisions of (b) do not prohibit incidental contact by the mask or helmet in the course of a conventional tackle or block on an opponent.
(2) A player who initiates contact against a defenseless opponent is responsible for avoiding an illegal act. This includes illegal contact that may occur during the process of attempting to dislodge the ball from an opponent. A standard of strict liability applies for any contact against a defenseless opponent, even if the opponent is an airborne player who is returning to the ground or whose body position is otherwise in motion, and irrespective of any acts by the defenseless opponent, such as ducking his head or curling up his body in anticipation of contact.

ARTICLE 8. USE OF THE HELMET. It is a foul if a player lowers his head to initiate and make contact with his helmet against an opponent

Return to general discussion

Appendix C: Risk curves from logistic regression (Study 2)

All events collapsed

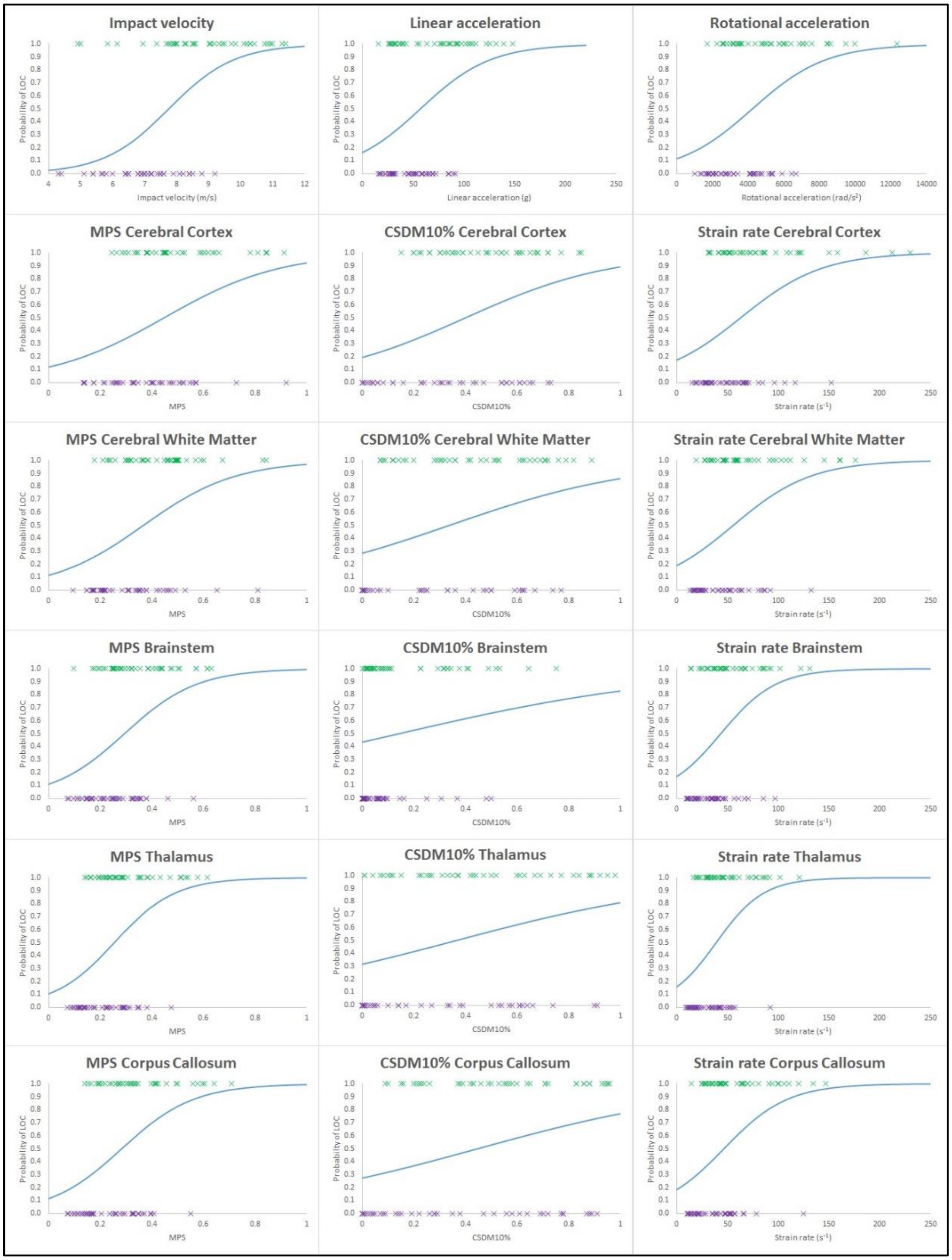

Figure 22. *Risk curves for dynamic response and brain tissue deformation describing the probability of LOC in American football concussive impacts (all events collapsed)*

Shoulders

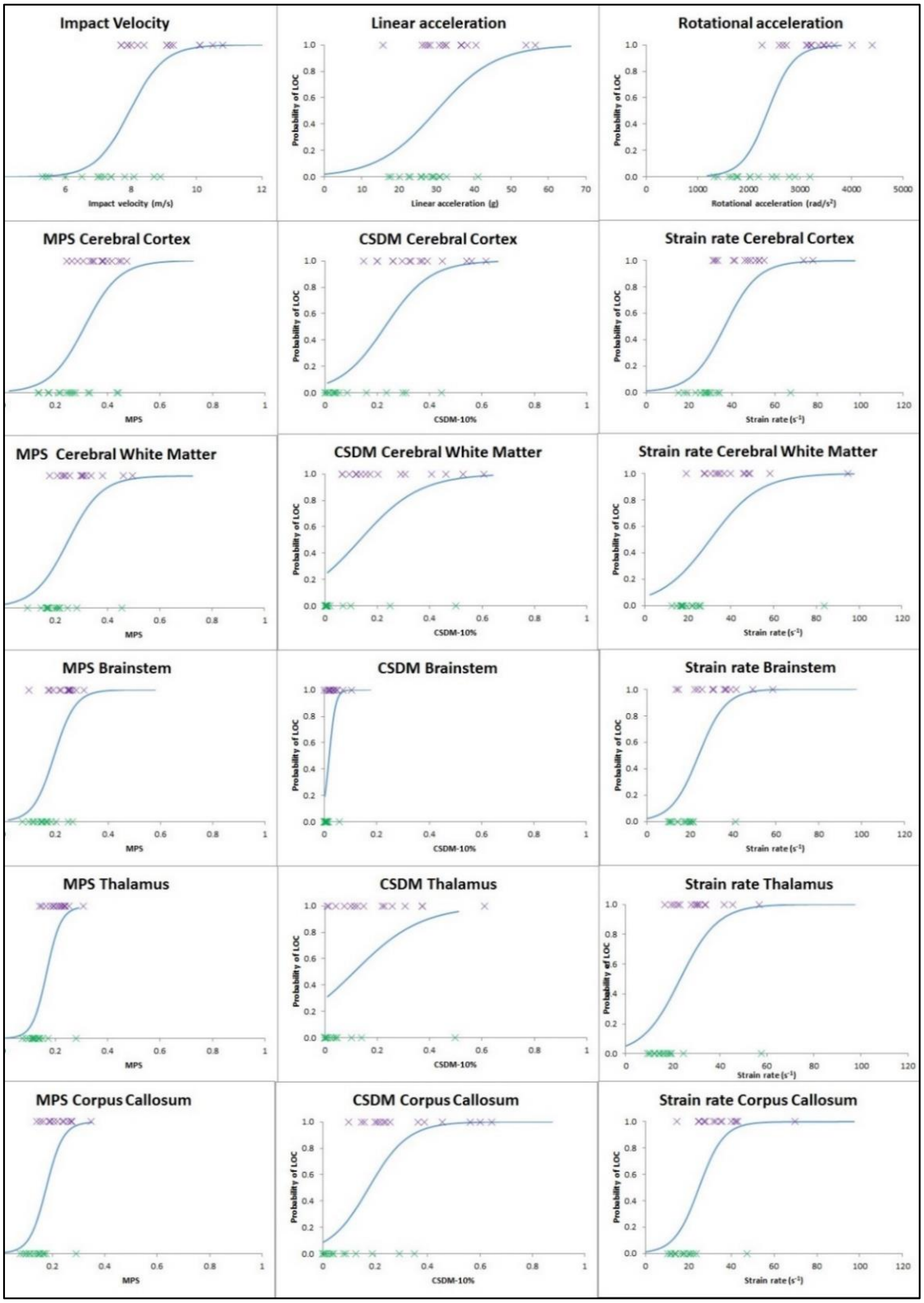

Figure 23. *Risk curves for dynamic response and brain tissue deformation describing the probability of LOC in American football shoulder collisions concussive impacts*

Helmet-helmet collisions

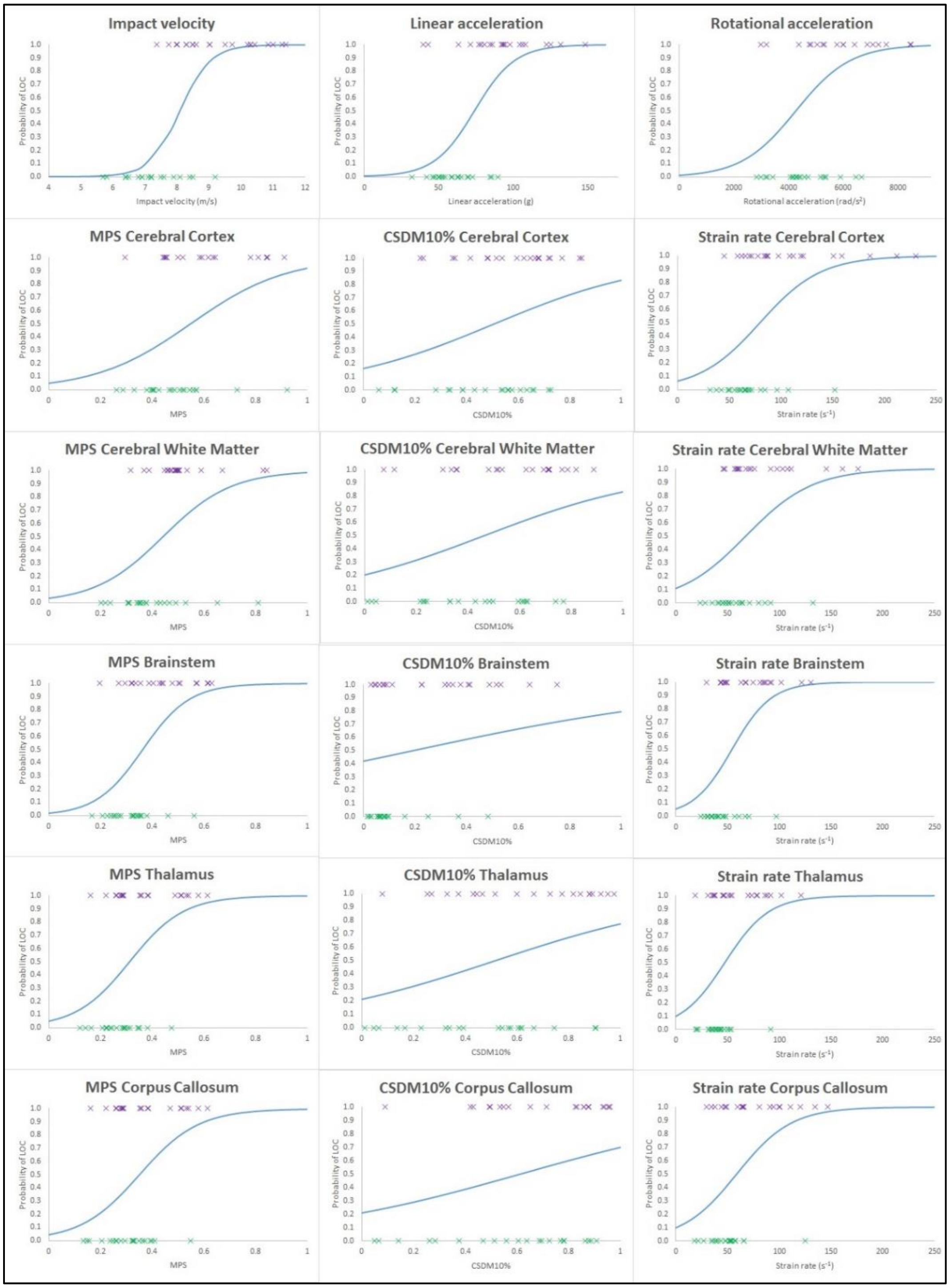

Figure 24. *Risk curves for dynamic response and brain tissue deformation describing the probability of LOC in American football Helmet-to-helmet collisions concussive impacts*

Appendix D: Histogram illustrating the comparison of LOC and no-LOC punches for peak linear and rotational acceleration

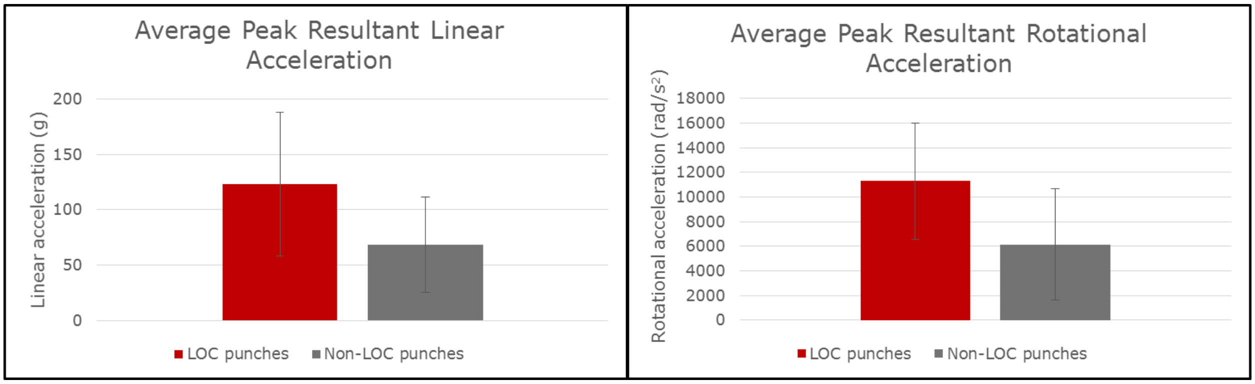

Figure 25. *Comparisons of peak linear and rotational acceleration (SD) between LOC and non-LOC punches*

Appendix E: Comparisons of data obtained in this thesis to data previously collected in Neurotrauma Impact Science Laboratory

Comparison of LOC and non-LOC punches to MMA concussive punches

Kendall (2016) reconstructed concussive punches from MMA fighting matches. These concussive punches were determined using visual cues of a concussion such as a loss of consciousness or loss of balance (Knockout and technical knockouts) experienced by the athletes. Peak linear acceleration reported by Kendall (2016) (75 g) was similar to the non-LOC punches (69 g) and lower than the LOC punches (123 g) reported in this thesis. A similar relationship was observed for MPS response where Kendall (2016) reported peak MPS in the brain as 0.50 compared to LOC punches (0.73) and non-LOC punches (0.47). However, the peak rotational acceleration (12 228 rad/s^2) reported by Kendall (2016) were closer to the LOC punches (11 279 rad/s^2) than the non-LOC punches (6145 rad/s^2). The differences in results despite using a similar reconstruction methods can be explained by the difference in impact characteristics. The average impact velocity measured by Kendall (2016) which is much lower than the impact velocities used in this thesis (11m/s±2 for hooks; 9m/s±1.5 for jabs). The striking masses used in this thesis were 2.3 and 4.7 kg whereas Kendall (2016) used 3.33 and 4.6 kg. The compliance of the boxing is larger compared to the MMA glove and the impact locations were different as well. Interestingly, Kendall (2016) included LOC as an inclusion criteria which resulted in high magnitudes of rotational acceleration similarly to those reported in this thesis.

Comparison to severe cases of concussive injuries: persistent concussive syndrome and Traumatic Brain Injury (TBI)

The results of brain tissue strain reported in this thesis are greater than the strain associated with persistent post-concussive syndrome (Post, et al., 2015). The authors reported an average of 0.38 which is closer to the average peak strain reported for the non-LOC concussion in this thesis (0.38). However, the authors used the University College Dublin Brain Trauma Model and comparisons across models should be done carefully. Interestingly, the values of maximum principal strain reported in this thesis are also greater than that of traumatic brain injuries reported by Post et al. (Post & Hoshizaki, 2013). This is likely due to the TBIs described by Post & Hoshizaki (2013) were mostly comprised of injury to vasculature and not to brain tissue. This provides further evidence that the mechanism of injury related to TBIs differ from the mechanisms responsible for concussive injuries.

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