Beyond the Hit: The Hidden Costs of Repetitive Head Trauma

Sikandar Khan and Lora Talley

University of the Incarnate Word School of Osteopathic Medicine, San Antonio, TX, USA.

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ABSTRACT: Repetitive head trauma in sports, particularly concussions, has been strongly associated with neurocognitive impairments, including depression, chronic traumatic encephalopathy (CTE), and altered brain function. These injuries can have significant consequences on major cognitive processes, such as learning and memory. This review synthesizes research that examines the effects of sports-related head trauma, particularly in football, on cognitive functioning. Post-mortem analyses of players across all positions have revealed neuropathological evidence of CTE, including a distinct reduction in hippocampal volume. Notably, episodic memory, a component of declarative memory, is frequently compromised in individuals with CTE. Furthermore, deficits in working memory may contribute to decreased performance during play. Early detection of head trauma and implementation of preventive strategies are crucial for mitigating long-term consequences. While impact-reducing techniques have shown some efficacy in decreasing brain injury incidence, proper tackling techniques, such as "heads-up play," also play a vital role in minimizing risk. Further research and increased awareness are needed to ensure athletes are fully informed of the potential cognitive risks associated with participation in high-impact sports.

KEYWORDS: Traumatic brain injury, chronic traumatic encephalopathy, concussions, football, national football league, centers for disease control, learning, pathophysiology, preventative, neurodegenerative

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CORRESPONDING AUTHOR: Sikandar Khan, University of the Incarnate Word School of Osteopathic Medicine, 7615 Kennedy Hill Dr., San Antonio, TX 78235, USA. Email: sek108@georgetown.edu

Introduction

Repetitive head trauma from sports, most commonly resulting in concussions, has been linked to neurocognitive dysfunctions such as depression,[1] chronic traumatic encephalopathy (CTE)[2] and altered brain functioning.[3] Concussions have also been shown to be detrimental to learning and those with neurocognitive issues such as attention deficit hyperactivity disorder[4,5] have a greater lifetime concussion history. Studies have shown that those with learning disabilities are more likely to sustain repetitive head injuries than other those without learning disabilities.[4,5] With previous studies by the National Football League (NFL) to understand how repetitive concussions affect long term brain health, it is crucial to look at how early-life concussions affect health over the long-term, especially on learning. It is also worth looking at how many concussions and which sport may cause which types of neurocognitive effects or if it is generalized between all sports. Repetitive head injuries are most often seen in sports such as football, due to the sheer number of athletes participating in the sport. The more the brain is exposed to rotational and accelerative forces, the more likely it is to see deficits in cognitive factors that need to be addressed to maintain a healthy brain. Repetitive head injuries have triggered a silent public health alarm[4] that needs immediate attention to prevent further drastic complications to player health and safety.

Traumatic Brain Injury (TBI)

Types of head trauma from sports or life accidents can vary in severity. These can range from a traumatic brain injury to skull fractures. A traumatic brain injury (TBI) can also range from mild to moderate to severe. Mild TBIs, also classified as concussions, involve scoring based on the Glasgow Coma Scale score of 14 or higher with the presence of 1 or more symptoms including loss of consciousness (not exceeding 30 minutes), amnesia of the injury not persisting for more than 24 hours, and altered mental status following injury.[6-8] Long term sequelae of TBIs include changes affecting thinking, sensation, language and emotions, as well as verbal learning and memory disparities and can depend on the region impacted by the TBI.[8] While these are generally documented symptoms for patients of TBIs, they are not always apparent to people whom have sustained a TBI. This may be due to lack of awareness of the definition and presentation of TBI by the general population. The Center for Disease Control (CDC) estimates a high prevalence of TBI in the United States population with approximately 214 110 TBI-related hospitalizations in 2020 and 69 473 TBI-related deaths in 2021.[9] These statistics paint an alarming picture on the prevalence of this injury. To put this into perspective, nearly 224 935 people pass away from unintentional accidents annually.[10] The CDC also notes those most commonly at risk for TBI's include adults 75 years or older.[9] Males are more likely to sustain, be hospitalized, and succumb from a TBI out of all the groups studied.[9] Falling, hit by or against an object and vehicle crashes were the leading causes of events leading to a TBI diagnosis.[11] Even though elderly adults are at the greatest risk, TBI's are the primary form of head injury in sports in adults.

Concussions

Due to increased exposure from media outlets, concussions have received national attention regarding head injuries. More commonly referred to in literature as mild traumatic brain injury (mTBI),[12] one can sustain a concussion from contact sports such as football, soccer, or hockey. In fact, a mTBI can be sustained from something as common as slipping and hitting your head on the ground. The University of Michigan estimates that 3.8 million concussions occur each year from sports.[13] This high prevalence highlights a need to further educate the public on brain injuries and preventative measures. During a concussion in football, an impact from a tackle or helmet-to-helmet hit subjects the brain to acceleration, deacceleration, rotational forces and elongation.[14] Alternatively, the CDC defines a concussion as conditions of temporarily altered mental status as a result of trauma to the head with or without loss of consciousness.[15] The amount of time spent unconscious contributes to the severity level of the concussion. Post-concussion, there are notable cerebral blood flow changes upon activation of brain areas being used, including increases in the frontal lobe and temporal areas.[16] These alterations in blood flow may take anywhere from weeks to months to recover from, and require varying degrees of rehabilitation.[8] Changes in blood flow can lead to associated symptoms including headaches localized to regions with decreased blood flow during activation, or use, of those areas upon metabolic demand, giving rise to post-concussion syndrome. Attention and difficulty concentrating also seem to be closely associated with reported symptoms, both temporary and long-term.[4,17,18] Most worrying for many athletes are the reported visuospatial and balance issues after sustaining a concussion,[19] as these issues can lead to poor performance after return to play. Persistence of symptoms depends on the severity of the mTBI.

In the National Football League and across all levels of football play, concussions are diagnosed quite frequently when compared to other sports due to the sheer number of athletes playing football over other contact sports. In one recent study, researchers analyzed football players who sustained concussions by their position, finding profile 1 consisting of quarterbacks, wide receivers and defensive backs having a significant effect on increasing strain and strain rate in the sulci.[7] This highly correlated with pathology in CTE.[7] Surprisingly, running backs were among the lowest positions with prior concussion rates of 33%, a number lower than kickers (46%).[7] This finding contradicts the generalization that running backs are known to "lower their heads" when playing. However, these results may be due to data collection characteristics such as underreporting. Additionally, other recent studies have found that position played at the highest level (NFL) was not associated with any relationship with CTE status or severity—suggesting that repeated non concussive injuries can be associated with CTE development.[20] While concussions are a major brain injury diagnosis, other types of brain injuries exist in sports as well such as second impact syndrome and coma.

CTE

Chronic Traumatic Encephalopathy is a condition that results from repetitive head trauma resulting in a progressive neurodegeneration.[2] Neuropathological presentation of CTE include cerebral cortex, medial temporal, and diencephalon atrophy with enlarged ventricles and mammillary bodies. Frontal lobe, medial temporal lobe, limbic, brainstem nuclei, and diencephalon all have accumulation of p-tau immunoreactive neurofibrillary and astrocytic tangles.[21] Also, axons and white matter bundles present with degradation.[21] Serious accumulation of proteins and loss of areas of the brain result in increased severity of CTE. CTE has only recently gained national attention through the work of many researchers, most notably Dr. Bennet Omalu. Dr. Omalu was the first to suggest the dangers associated with repetitive head trauma in football players, especially NFL players. However, it was noted that CTE was first reported by Harrison Martland in 1928 when he described the symptoms presenting in boxers.[21] Dr. Omalu brought the focus to football, a sport that owns a calendar day of the week. He found on autopsy that in deceased players' brains, there were notable diffuse amyloid plaques and sparse neurofibrillary tangles in neocortical areas.[22] The accumulation of amyloid plaques and neurofibrillary tangles can disrupt the normal functions of the brain's blood vessels and can eventually erode the vessels, leading to complications such as mood disorders and dementia.[23] These symptoms have even manifested as contributing to cases of suicide, necessitating this disease as a public health crisis. Other symptoms of CTE are initially subtle, but progressively worsen including irritability, impulsivity, aggression, depression, short term memory loss, explosivity, and suicidal ideations.[21] Behavior explosivity is particularly associated with behavioral presentations of CTE. A notable cognitive presentation of patients with CTE is impaired episodic memory.[24] Thus, CTE is an injury that needs urgent attention to design preventative measures. With a variety of symptoms and presentations associated with CTE, there is concern and little research about how this disease affects learning. CTE is also defined by the accumulation of tau proteins in neurons, which is unique from other neurological diseases such as Alzheimer's.[2,21] The ability to distinguish CTE from other neurodegenerative diseases is critical in determining its prevalence in diseased donors. However, some presentations of CTE are comorbid with other neurological diseases such as Alzheimer's furthering the difficulty and challenge in separating its long-term effects. McKee et al.[21] found in their study that, in 37% of their cases, patients presented with motor neuron disease, Parkinson's, Alzheimer's, and frontotemporal lobe degeneration. The researchers suggested that this comorbidity may be due to repetitive head traumas activating molecular

pathways that produce and accumulate proteins such as TDP-43, α-synuclein and amyloid-β seen in such diseases.[2,21] The overproduction of these proteins can lead to aggregation in certain areas of the brain and cause the symptoms of the diseases and CTE. If these proteins accumulate in the inferior temporal lobe and amygdala, symptoms include bursts of aggression, irritability, and impulsivity can occur in CTE presentations.[21] Incidentally, accumulation in the nucleus basalis of Meynert and septal nuclei may also contribute to cognitive symptoms.[21] Additionally, aggregation in the inferior orbital frontal cortex and brainstem are attributed to depression symptoms. Sustained aggregation in the anterior thalamus and hippocampus can contribute to memory loss, cognitive impairment and dementia.[21] Currently, CTE can only be diagnosed through examination of brains once the patient is deceased. However, recent studies have suggested certain biomarkers may be able to discern this disease in living individuals.[25]

Pierre et al.[25] noted in their review that magnetic resonance imaging (MRI) can be used to help aid in the diagnosis of CTE, however some of the structural changes are not solely associated with CTE. MRI can be used to detect things like diffuse axonal injury and more soft tissue differences, as compared to computed tomography (CT).[25] However, a specific technique of MRI, diffusion tensor imaging (DTI) has shown some correlation with prognosis of mTBI.[25] This method evaluates the orientation and integrity of white matter tracts, which are often injured in mTBIs and thus CTE. This would be a helpful tool in the efforts to detect CTE early.

Pierre et al. also investigated many other modalities that were helpful in detection of CTE in alive patients. Another such imaging technique that they found helpful for CTE detection that happened to also use NFL players was magnetic resonance spectroscopy.[25] This method measures metabolic activity within the brain, based on the chemical shift of protons.[25] Injured areas thus show decreased activity. The study demonstrated this decrease in activity with lower creatinine in the parietal white matter.[25] Considering this information, one might suspect functional magnetic resonance imaging (fMRI) would be of use too. This was not the case as noted by Pierre et al.,[25] that showed that since players with CTE may already have decreased cerebral blood flow, thus confounding the results of an fMRI.

Another imaging modality that Pierre et al. found that may be of beneficial use in antemortem was susceptible weight imaging (SWI). This method uses the different responses to molecules that may occur in a magnetic field in order to detect changes.[25] As it relates to mTBIs or CTE, one could use this method to detect diffuse axonal injuries or microhemorrhages, which have been demonstrated in contact sport players mTBIs, especially repetitive mTBIs.[25]

Biomarkers have been of interest for some time in the clinical use of detecting CTE antemortem. Thus, positron emission tomography (PET) CT has garnered much interest in the CTE field. One biomarker of interest is FDDNP, which specifically binds to proteins associated with CTE, but it, unfortunately, has also been shown to bind other neuroproteins such as beta-amyloid and hyperphosphorylated tau making it hard to distinguish from other neurodegenerative diseases such as Alzehiemer's.[25] Therefore, specific markers for CTE are of heavy interest. Pierre et al. found that [18F]AV-1451 (flortaucipir) is one of particular interest and specificity to CTE. Their review found studies that tracked this biomarker in former NFL players with reported neuropsychiatric symptoms was significantly found in areas associated with CTE, found even in one case study 4 years before a post-mortem diagnosis of stage IV CTE.[25] If more studies are able to utilize this protein and validate a clinical correlation, this biomarker could be heavily useful in early detection and management of CTE sequelae. Many other biomarkers are also being investigated but have yet to show any such promise as they are confined to similar significance factors as the flortaucipir studies.

In addition to imaging studies, fluid biomarkers are also being deployed in the early detection of CTE. Some such biomarkers include p-tau, triggering receptor expressed on myeloid cells 2 (TREM2), chemokine ligand 11 (CCL11), neurofilament-L (NfL), and Glial fibrillary acidic protein (GFAP).[25] With CTE being defined as an accumulation of p-tau proteins, p-tau can be of use, but not solely for the diagnosis of CTE as it also seen in other neurodegenerative diseases.[25] TREM2 is an inflammatory maker that is found in cells of the nervous system such as microglial cells, peripheral macrophages and dendritic cells.[25] In the Pierre et al.[25] review, they found that a study showed a positive correlation between TREM2 and t-tau proteins in the CSF of former NFL players with reported related symptoms of mTBIs. However, this protein is once again seen in other neurodegenerative diseases. CCL11, a chemokine, plays an important role in immune responses, such as promoting pro-inflammatiory mediators like the ratio of cytokine interleukin (IL)-4 and interferon (IFN)-γ in brain cells such as microglia and astrocytes or the choroid plexus and CSF.[25] However, these increases in CCL11 were seen in post-mortem studies and need further investigation into pre-mortem players. NfL and GFAP can be used as an indicator of axonal damage,[25] but further studies need to elucidate them from other neurodegenerative diseases.

CTE Pathophysiology

There are 4 stages to CTE pathology, with symptoms increasing in severity from I to IV. According to McKee et al.,[14] Stage I is mostly unremarkable, with infrequent neurofibrillary tangles (NFTs) along with symptoms including headache, short-term memory difficulties, diminished concentration, and depression. Stage II shows more subtle signs of disease including enlargement of certain areas of the brain including the third and fourth ventricles and substantia nigra.[14] NFTs in the substantia nigra are concurrent with symptoms from stage I

with the added concern of prominent behavioral and personality differences.[14] Stage III brains showed all stage II pathology and include reduced weight from atrophy of the frontal and temporal lobes.[14] NFTs remain present in the temporal, frontal and parietal cortices, hypothalamus, substantia nigra and substantial NFTs in the hippocampus, entorhinal cortex, amygdala, nucleus basalis of Meynert, and locus coeruleus in stage III.[14] Symptoms associated with stage III include all stage II symptoms with the addition of memory loss, executive dysfunction and aggression.[14] Stage IV presents with all of the previous pathologies except brain weight is significantly lower due to significant atrophy in the frontal, temporal, medial temporal, anterior thalamus, and generalized white matter.[14] Additionally, generalized neuronal loss occurs with severe degradation in the substantia nigra[14] along with neurofibrillary degradation in the hippocampus, amygdala, and temporal cortex. NFTs are widely aggregated in the hippocampus as well.[14] Severe symptoms can include executive dysfunction, memory loss, dementia, language difficulties, gait, and visuospatial difficulties.[14] A number of patients who suffered from CTE Stages II-IV, particularly those with Stage IV, have a high likelihood of passing away from suicide, drug overdose or alcohol abuse.[2,14] This finding suggests that as the disease progresses, the outcome becomes worse for the patient. While some patients suffering from symptomatic CTE disclosed a history of multiple repeated concussions, others did not. Since the study primarily analyzed donated brains from football players, this finding suggests that participating in the sport itself could put athletes at a higher risk for developing CTE, even if they are asymptomatic.[26] While the study focused on football players brains, some of these pathologies were seen in other sports like soccer, rugby and ice hockey.[14]

The pathophysiology of CTE is still not fully understood. As noted by Turner et al.,[27] some key questions such as the inter-injury interval, number and severity of impacts, age of impact, mechanism of impact, biomechanical mechanisms, genetics role, gender influences, environment effect, and preconditioning are all factors that require further study to elucidate their role in CTE development. In regards to inter-injury interval, many studies differ upon the time of repeated impact that would cause further damage and sequelae down to CTE stages, making return to play timelines difficult to pinpoint. However, most of the reviewed studies agreed that the longer the time between impacts, the less chance there was for an additive effect to occur.[27] Timelines have varied from 24 hours to 30 days, further complicating this timeline. Turner et al.[27] also found in their review that location of the repeat injury also plays a role as damage to a different area of the initial injury in animal models did not worsen outcomes. This finding, while needing additional elucidation, adds to the complexity of teasing out the injury-interval phase. With regards to the number and severity of impact, repetitive injury did come to a consensus that repeat injuries has a detrimental effect on the animals, especially in early time frames.[27] However, severity also played a role and as noted previously, once an impact is sustained, this makes one susceptible to additional hits even at a lower level of force.[27] This again highlights the complexity of managing return to play guidelines. As one might logically conclude, the earlier one sustains a TBI, the worse the outcome may be and was shown as one of the biggest risk factors in this development. Since the brain is still being developed at early ages, early exposure to a developing brain may lead to worse outcomes.[27] However, as Turner et al.[27] noted, it is unclear whether elderly populations would have a worse outcome especially in populations that have pathology already on board. Further studies need to look further into the age related outcomes in order to establish a better guideline and management prediction. One question that Turner et al. had that may have been addressed in other studies such as Quigley et al.[28] is the role of linear and rotational impacts. Further studies need to be done to tease out how each of these forces impact the prognosis of mTBIs and CTE. In regards to biomechanical mechanisms, much effort has been placed here recently, notably in the Myer et al. study. However, as pointed out by the authors, not all of the biomarkers being studied were solely for CTE and future studies need to determine more exclusive biomarkers in CTE. In regards to genetics, as seen in other neurodegenerative diseases, APOϵ4 and APOϵ3 have been indicated with worse outcomes in CTE or TBI.[27] However, these markers are also seen in Alzheimer's Disease further showing the need for a more specific and sensitive marker for CTE. Gender also plays an interesting role in both the impact and severity of TBIs. However, as Turner et al.[27] noted, this area is controversial as there has been limited research and noted cases of CTE in females. One explanation for this, as highlighted by many studies is the fact that most young adults that sustain TBIs are males due to the risk taking activities with sports such as football and military exposure. However, Garringer et al.[29] found a reduction in estradiol in females with TBIs that has yet to be further explored. Insight, or lack thereof, into hormonal changes and their effect on TBI or CTE development should be of interest in future studies as the role of hormonal changes is seen in elderly females and the development of neurodegenerative diseases. Another area that needs further research is the role of the environment after sustaining a TBI, especially in areas such as diet, social support, supplements and drug or steroid use. As one might suspect, better social support has shown better outcomes, particularly decreasing the likelihood of post concussive syndrome symptoms.[27] Diet, however, has yet to have enough studies, if any, in its role in TBIs.[27] Similarly, since some former athletes, like those in the NFL, have used steroids and developed CTE, this association needs to be studied further. Finally, preconditioning is also an area of interest that needs to be further elucidated. Preconditioning is when someone obtains an injury, like a TBI, and it serves as neuroprotection for an additional injury. This mechanism is based in protective antioxidants that are released

by neurons following an injury like a TBI.[27] However, while in theory it seems protective, the actual protection in CTE development is unclear. While seen as protective with in vitro studies, it has yet to be understood its role in human populations and CTE development.

Additionally, developing models to study and replicate the full effects of traumatic brain injury (TBI) has encountered numerous challenges. While many in-vitro studies have shown promising results, accurately recreating the extent of damage experienced by humans remains difficult. Moreover, the use of appropriate controls presents additional limitations in designing models for therapeutic research. For instance, rodent studies require similar anesthesia induction and timing for both control and intervention groups, complicating experimental consistency. These challenges, along with the factors highlighted by Turner et al., underscore the importance of identifying biomarkers. Biomarkers can aid in the development of models that utilize biochemical, electrophysiological, and advanced imaging techniques to more effectively assess neural injury.

Physiology of Learning

The process of learning is a complicated process. From early life, the brain is constantly developing new neural connections and synapses. Memory is one of the processes that consolidates learning to help us understand, learn, and perform everyday functions. Two major processes of memory well defined in the literature are known as declarative and nondeclarative memory.[10] Declarative memory is used for retrieving and storing facts, whereas nondeclarative memory is used for procedural events such as riding a bicycle or putting on clothes. While it is true that no single area of the brain is solely responsible for memory, a majority of memory storage and retrieval occurs in the hippocampus.[30] Localization of memory was most notably evident in the famous case of patient HM, whose hippocampus was removed as a treatment for epilepsy. HM suffered from anterograde and partial retrograde amnesia, suggesting that the hippocampus is strongly associated with memory and long-term potentiation (LTP).[30] Reduced brain volumes and protein aggregations in the hippocampus have been associated with conditions such as Alzheimer's disease, where memory loss is significant.[30] Decreased hippocampal volume is also a distinct neuropathological finding in CTE. Episodic memory, a subset of declarative memory, is also seen to be affected in CTE pathologies. Episodic memory resides primarily in the hippocampus, entorhinal, and perirhinal cortices, with severe pathologies of each area noted during the latter, more severe stages of CTE pathology.[2] These alterations to the hippocampus lead to memory problems, suggesting the impact asymptomatic CTE may have on people's ability to properly learn.

Another type of memory, working memory, is an important function involved in decision making and behavior. This type of memory maintains short-term information to integrate it with high-order cognitive processes to execute plans and behaviors.[31] Areas involved in working memory include the hippocampus, parietal and prefrontal cortices.[18] Shah-Basak et al.[18] noted that visual working memory and attention are intricately correlated with each other to help filter out relevant visual information. In football, this would manifest as tracking down a football to be caught by a player or memorizing football plays. Disruptions to this could lead to inability to filter out this information to track down the football or not performing the correct play, and further learning the plays properly. Hyper- and hypo-activation were noted in some players with a history of concussions during the Shah-Basak et al. study, causing concern to working memory tasks.[18] In the non-sports world, this could lead to such drastic effects as losing concentration or inability to filter out irrelevant information while in class, thus highlighting the significance of damage to this memory system.

Early Detection

Previous analysis done by researchers has allowed for detection of concussions through bloodwork. Dr. Brolinson and his colleagues at the Edward Via Virginia College of Osteopathic Medicine (VCOM) and Virginia Polytechnic Institute and State University (Virginia Tech) are among the key researchers in the field of concussions working with many to help detect and prevent the prevalence of concussions. Since CT and MRI scans do not always show structural signs of brain damage, a new method necessitates development. Through a collaboration between Dr. Brolinson and Banyan Biomarkers, a means to detect key proteins which can depict the signs of brain damage was developed. The targeted proteins, glial-fibrillary-acidic-protein (GFAP), ubiquitin-C-terminal-hydrolase-L1 (UCH-L1), and microtubule-associated-protein-2 (MAP-2), are elevated, as would be the case in a patient undergoing a heart attack.[32,33] Dr. Brolinson and his colleagues at VCOM and Virginia Tech have been at the forefront of football helmet design, their innovative redesigns have been associated with a decrease in the number of reported concussions in football.[32]

Preventative Measures

Over the years, helmets have evolved to counter concussion prevalence and make football a safer sport. While originally designed to prevent skull fractures, spinal injuries and neck injuries, recent technology has helped reduce the rate of concussions in football through research done at Virginia Tech.[32,34] Dr. Brolinson at Virginia Tech was able to conduct a study using accelerometer sensors to monitor the acceleration of the brain during practice and games.[34] During a potential concussion-inducing hit in football, the amount of gravity forces (g) exerted on the brain are 98 g.[34] For context, the amount of g forces sustained during a sneeze or heading a soccer ball are 4 g and 38 g, respectively.[34] A helmet that can help lower concussion forces needs to be developed in order to address the

concussion epidemic. The researchers developed a Summation of Tests for the Analysis of Risk (STAR) rating for a helmet's ability to reduce these forces and acceleration as well as still protect from the original serious injuries.[34] Based on a ranking of 1 to 5 stars (5 being the highest and best at reducing the forces of acceleration), the most effective helmet on the market reduced at hit that would reduce a 150 g hit to 75 g.[34] At Virginia Tech alone, the amount of concussions have been reduced by half after using the recommended helmets and techniques.[34] After the initial study, Virginia Tech continues to release yearly helmet STAR ratings for the public. Organizations ranging from the Pop Warner youth football league to the NFL utilize this system for their players.[34] This preventative measure helps address the epidemic by lowering the concussion rate and protecting players.

Recent attention has also been drawn to return to play protocols to help aid in preventing long term complications of concussions. Citing how concussions can impact learning, researchers urge the public to address this epidemic that is impacting its football players and repetitive head injury sports.[4] It also highlights adding laws to updated return to play protocols, concussion training for medical staff, education for athletes and non athletes.[4] Highlighting how negative postconcussive symptoms can be to a students academic performance need to be stressed so that both those that sustain concussions and those who are around them can properly address the whole person in their post-concussion care.

Although there have been vast improvements to helmets, helmets are the last line of defense in preventing a concussion. To help prevent concussions, combined efforts to practice better technique and coaching are crucial to drastically improving concussion prevalence. If players are able to practice and have muscle memory for proper technique, the less likely they are to sustain concussions from bad hits. Researchers monitored player's helmets using sensors in a small study on young children, finding hits with levels close to concussions.[34] As a result, rule changes along with decreased contact and tackle drills were implemented in the children's Pop Warner league nationwide.[34] Monitoring concussions and changing rules will help determine exposure to head injuries in the long term. Recent use of padded helmet shells, coined the *Guardian Cap*, are cited by NFL officials to show some promise in preventing concussions in the preseason, but further analysis yields mixed results.[35] The mixed results further point to the helmets being the last line of defense in combating head trauma.

Another deterring factor that should be made more readily available to football players are the results found in the Navarro et al. study. This study discovered that NFL players who sustain a concussion were more likely to have shorter playing careers, salary reductions, and worse performance post-concussion.[36] Players with this data can then learn to practice better technique and avoid risky play. However, this also may deter players from reporting symptoms of concussions.

Further, recent studies show that the combined number of head impact and cumulative impact of the hits further lead to the risk of the development of CTE.[20] This study attempted to address the challenge of quantifying the amount and types of hits to the head that lead to an increased risk of developing CTE. They also noted that definitions of concussions, as well as length of play is also difficult to assess when players present with asymptomatic presentations.[20] While underreporting may contribute to lower concussion reporting, asymptomatic or non concussive injuries have been associated with CTE development.[20] This finding highlights the need to practice heads up tackling emphasis to lower the repetitive blows to the head, both at the concussive and sub concussive levels, these players so very much need in order to avoid developing CTE.

Recent Protections

The Q-Collar, also known as a jugular vein compression collar,[37] and the Guardian Cap[28] represent recent innovations aimed at reducing the prevalence of concussions in football. The jugular vein compression collar introduces a novel strategy compared to traditional methods of mitigating brain injuries. Its mechanism is based on the principle that compressing the jugular vein increases the volume of venous capacitance vessels, thereby enhancing the reserve volume within the brain and spinal column.[37] This leads to greater brain stiffness, making the brain more resistant to the high-impact forces that cause injury.[37] This concept stems from the slosh mechanism, which observes that a container filled with fluid absorbs less energy than one with a smaller fluid volume.[37]

In a study conducted by Myer et al.,[37] high school football players wore the collars during a season, with head impacts tracked using a G-Force Tracker. Diffusion tensor imaging (DTI) biomarkers were used to measure changes in white matter, which have been linked to post-concussive symptoms.[38] The study revealed that players wearing the collars experienced fewer decreases in white matter density in regions such as the corpus callosum, anterior and posterior internal capsule, corona radiata, posterior thalamic radiation, external capsule, cingulum, and superior longitudinal fasciculus, compared to controls.[37] These findings suggest the Q-Collar holds promise in mitigating concussion-related brain injuries.

Guardian Caps, on the other hand, have gained popularity as an additional protective measure, particularly during NFL pre-season games and practices. Unlike the Q-Collar, Guardian Caps focus on enhancing current helmet designs by adding extra cushioning to reduce high-impact forces during gameplay. However, a study by Quigley et al.[28] found that Guardian Caps did not significantly reduce or attenuate peak linear or angular acceleration—key contributors to concussions and related symptoms. Despite these findings, the NFL reported a 50% reduction in concussions associated with Guardian Cap use, though the source of this data has not been published.[28]

The NFL's Battle

For years, the NFL fought to counter studies suggesting a link between CTE and football through their own research that undermined this connection.[23] These studies were not reliable because they produced false results between the connection in order to deny it. During the first presentation from Dr. Omalu, the NFL quickly disregarded Dr. Omalu's data and started its own research. It was only as of 2016 that the NFL acknowledged the link between the two. In July of 2017, Boston University published a study showing that of the 111 brains donated to them for study from former NFL players, 110 showed signs of CTE.[23] This study further cemented the link between CTE and football and the widely accepted link between the two in the scientific community.[23] Recently, as of 2022, the NFL admitted to a drastic rise in concussions during the 2022 season.[39] A compelling argument noted in multiple studies indicated that the presence of learning disorders and disabilities are correlated with higher rates of multiple concussions and risk for future concussions.[4,7] However, this is not to say that learning disabilities such as attention deficit hyperactivity disorder (ADHD) cause increased risk of concussion. The researchers simply noted that they reported more baseline concussion symptoms than controls without learning disabilities.[4] This work suggests that those with these disabilities need tailored assessments when experiencing brain injuries.

Discussion

As the amount of years of play and number of repetitive head injuries occurring through any level of football increases, the more at risk one is likely to be diagnosed with CTE or a concussion.[2] The more concussions or repetitive head injuries, including nonconcussive injuries, an athlete sustained, particularly if it was three or more, the more likely they were to sustain another concussion.[40] A study that looked at high school athletes, particularly football players, noted that a history of three concussions were more than nine times more likely to report at least three classical symptoms of concussions after sustaining another injury.[40] This reflected that the more concussions in an athlete's history, the lower the threshold may be to sustain a concussion going forward and experience more symptoms. A proper definition of concussion needs to be established and presented to all athletes at a higher risk of sustainment. By expanding the definition, more symptoms can be reported and detection of concussions can occur.[39] To more reliably diagnose and report concussions, clinicians and athletic personnel need to provide the definition to athletes upon report or pre-season during baseline testing. During baseline testing, clinicians can be sure to incorporate a full definition and explain the symptoms of concussions. Measurement of impacts through force monitors can also help draw attention to athletes who may sustain non concussive blows. A treatment option used to treat patients of TBI in rehabilitation is photobiomodulation using low-level laser therapy.[41] Photobiomodulation stimulates cells to generate and undergo self repair through the use of non-invasive and non-thermal infrared light.[41] In studies, low-level laser therapy has shown to significantly improve memory, attention and mood.[41] The therapy does this by penetrating into the brain tissue, modulating brain plasticity and affecting formation of molecules such as ATP, DNA, RNA, NO, and changing the redox state in mitochondria to regulate transcription factors.[41] These changes increase blood flow and ATP levels to improve the oxygenation of the damaged areas. While promising, more research is needed to find more practical and readily accessible treatments for TBIs, with further attention on preventative measures.

Conclusion

Many studies have linked playing football to head injuries such as TBIs, concussions and CTE. The longer a person plays football, the more likely they are to sustain one, if not multiple, mTBIs and furthermore CTE. CTE comes with a variety of symptoms, cognitively and behaviorally, that affects memory functions. Changes to the hippocampus and working memory areas due to protein aggregation and decreased volumes lead to these memory changes and loss.

NFL players with longer careers were more likely to be diagnosed with stage IV CTE postmortem. Changes to helmets, techniques and coaching have caused concussion rates to decline, but still remain a prominent injury in football. While it may take a decade for symptoms to show in retired football players, the prevalence still highlights this public health crisis as many players diagnosed with stage II-IV CTE commit suicide. In order to improve outcomes, studies need to look at how to improve symptoms until a better prevention method is able to drastically reduce concussions and brain injuries. While the Q Collar offers some hope for improvement, it does not offer total prevention. The brain is the most complex and vital organ, and diagnosing a concussion is even more complex-No one concussion is the same as any other. Until research finds a fully preventative measure to combat the g-forces during football hits, the NFL along with the sports world will forever face an endemic public health crisis and a boogie man in its closet.

Author Contributions

Sikandar Khan- Researched and wrote the manuscript during The Georgetown University Master's in Physiology and Biophysics Program and during The University of the Incarnate Word School of Osteopathic Medicine Doctor of Osteopathic Medicine Program. Ryan Downey- Edited and supported the manuscript during Sikandar Khan's time at The Georgetown University Master's in Physiology and Biophysics Program. Lora Talley- Edited and supported the manuscript at the University of the Incarnate Word School of Osteopathic Medicine.

Ethical Considerations

Ethical approval was not required.

ORCID iDs

Sikandar Khan https://orcid.org/0009-0009-1034-9349
Lora Talley https://orcid.org/0009-0001-1395-5557

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