Cognitive effects associated with frequency and onset of sports related concussions

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COGNITIVE EFFECTS ASSOCIATED WITH FREQUENCY AND ONSET OF SPORTS RELATED CONCUSSIONS

by

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MARK DOERR

ABSTRACT

Social interest and recent advance in technology have made concussions on the largest topics in scientific research today. Knowledge continues to be uncovered and more data and information is studied on the effects of concussions and links to later in life cognitive decline. Dementia and Alzheimer’s disease have been known consequences of chronic traumatic encephalopathy but with recent findings in retired football players, more research is needed to show the correlation between concussions and the effects on cognition. Furthermore, with millions of youth athletes participating in sports each year, the impact of concussions on development and maturation need to be further researched. Initial retrospective studies seem to show the correlation between early in life concussions and decreased cognitive function later in life but longitudinal studies are lacking. Cognitive function data collected in longitudinal studies may help to show how early changes in function may be able to be identified and prevent further decline from repetitive impacts. Studies such as this would help fill the gap in research that could change youth sports as well as medical treatment and prevention to youth concussions.
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INTRODUCTION

Background

Youth sports programs are very popular throughout the United States. Football continues to be a mainstay in American culture with participants joining youth programs as young as seven years old. Per Pop Warner, one of the nation’s largest youth football organizations, more than 250,000 adolescents play football every year. The number continues to grow as children age with over one million students participating in high school football every fall.¹ With the increased number of participants, comes an increase in head trauma. It is estimated that 117,000 diagnosed concussions were seen in emergency departments from 2002 to 2012 in the United States, 41% due to head to head contact in football. This number is considered to be an underestimated as many concussions go undiagnosed with estimated 81-92% of concussion do not result in loss of consciousness.²

A concussion is defined as a brain injury caused by energy being transmitted to the head from direct or indirect contact with the head, face, or elsewhere. This energy results in the impact of the brain against the skull or in a strain of the tissue and vasculature.² Common symptoms of acute concussions are similar amongst children and adults, including behavioral changes, cognitive impairment, sleep disturbances, headaches, and emotional lability.³

Although the amount of concussion research is growing rapidly, the majority of is focused on adults. Much of this has to do with the focus by mainstream culture on the NFL. Yet, children continue to be under represented in research as approximately 65% of
pediatric concussion are results of sports and recreation. 4 Previous research once thought that pediatric concussions healthy quicker and have less long term effect, but recent data has begun to show the opposite. Studies have shown that persistent behavioral deficits have been recorded one year after injury. 5 Even more recent data, Moore et al. 2015, showed children injured early in life exhibited the largest deficits with changes in attention and executive control noted two years following concussions. 6

**Statement of the Problem**

Concussion research has vastly grown over the last twenty years but more specific studies on pediatric brain trauma are needed. Although youth sports leagues continue to adjust the rules of play to increase the safety of the athlete, it is still unknown if this is enough to prevent long term impairment. Recently, the National Youth Football League implemented rules changes that include having every coach certified with the CDC Heads Up Concussion training. This is a great step in increasing the awareness of concussion symptoms and allowing children to get treatment in the shortest amount of time. Yet, this does not protect against the original head trauma. Pee Wee Football has recently made changes to their rules to help reduce the amount of head to head contact during games and practices. Recently, contact was prohibited during two-thirds of practice time and drills involving head on blocking and tackling were eliminated. They also have strict weight restrictions for each division, which reduces the amount of force a smaller child will absorb. 7 All of these rule changes are important steps to reducing the amount of head trauma to youth athletes, but it is still unknown the effects of a single concussion or repetitive impacts have on the maturing brain.
Hypothesis

A participant in youth football, starting at the age of ten, will have lower cognitive function and behavioral impairment when compared to an adolescent who does not play contact sports over the course of their brain maturation.

Objectives and specific aims

The purpose of this study will be examine the impact of concussions and head injuries during the development of athletes. Concussions continues to be highlighted with new research and data being published yearly. This data continues to shape the nature of contact sports, especially in young adults and adolescents. With the large amount of attention concussions have received due to mainstream sports, it is important to study the effects of head injuries on developing athletes. Unfortunately, little is known of the impact to future cognitive function as athletes mature into adulthood. This study would help to fulfill the gap in knowledge concerning impacts on young athletes as well as stage as a starting point for longitudinal studies on cognitive function into adulthood.

- To create a longitudinal study following youth athletes starting at age ten until age 25 for complete brain maturation.
- Focus on football only compared to non-contact youth to focus on specific causes of brain trauma
- To study how early life concussions influence delays in cognition and behavioral health.
- Establish a risk ratio for exposure to concussions and cognitive changes.
REVIEW OF THE LITERATURE

Overview

Traumatic brain injury (TBI) is a serious cause of disability to young adults worldwide. Concussions are no exception. Concussions originally were defined as brain trauma from a low velocity collision that results in brain shaking. Following more detailed research in the past 10 years, concussions have evolved into a complex pathophysiological process involving the brain tissues, vasculature, neuronal tissue and metabolism. Concussions can be caused by either direct collision with the head, face, neck, or body with forces being transmitted to the head. Overall, subjective symptoms generally resolve in the first 7-10 days. Symptoms generally include headache, cognitive fog, and emotional lability. Physical manifestations include loss of consciousness and amnesia following the impact. Loss of consciousness should not be used as a diagnostic tool though, as 81-92% of concussions do not result in patient losing consciousness. Patients also frequently note behavioral changes such as irritability and cognitive impairment such as slowed reaction times.

More than 85% of TBI are considered mild TBIs (mTBI) or concussions.

Concussions are generally thought as minor injuries with almost 85% of patients making subjective symptomatic full recoveries within the acute phase of 28 days. Current research does not indicate that one concussion will result in significant morbidity, but the effects of multiple impacts remains less clear.
Epidemiology

The increased awareness in contact sports, and the increased incidence of blast related trauma due to war have escalated the public concern and urgency to understand the mechanisms of TBIs and work towards obtaining a therapeutic outcome. Concussions may occur in any sport but have a much higher frequency in contact sports such as football, rugby or soccer. It is estimated that 1.6 to 3.8 million TBIs occur each year \(^4\). Approximately 80% of all TBI cases are considered mild due to the lack of external symptoms such as cognitive, motor or somatosensory function deficits \(^8\). Due to the silent nature of majority of concussions, it should be noted that this estimate may be lower than actual occurrences, considering as many as 50% of concussions do not seek medical attention \(^7\).

Since contact sports make up the majority of causes for concussions, football, basketball and soccer have been studied the most extensively. With an estimated 4.5 million amateur athletes participating in football each year, the focus on concussion in football has never been higher \(^9\). It is estimated through Dr. Daneshvar and et al. that 50% of amateur athletes that were surveyed suffered one concussion during the season and 30% sustained multiple diagnosed concussions \(^1\). Although, greater strides have been made to be vigilant to the signs of a concussion, these numbers may continue to be underestimated as players and coaches do not report all instances. Even more concerning, helmet based accelerometer studies have estimated that high school players may receive 600 subconcussive impacts and college athletes sustaining over 1000 each season \(^9\). This
topic will be discussed later in the paper but it is important to note that these repetitive impacts may lead to neurological consequences as the athlete ages.

Children continue to be at higher risk due to athletes participating in multiple sports year round. Furthermore, organized youth sports continues to grow as participation can occur as early as four years old. From 2002 through 2012, it was estimated that over 100,000 non high school youth athletes, ages 4 to 13, were evaluated in emergency rooms across the United States. This number again is likely underestimated as athletes were not diagnosed or may have been treated by medical professional outside of the included hospitals. The mean age of concussions recorded for non-high school for male and female athletes was 11 years old. This correlates with the maturity of the athletes as players become bigger, faster and more aggressive. Rules also begin to change as players are allowed to tackle in football causing increase risk of subconcussive and concussive impacts. Male athletes also make up almost two-thirds of diagnosed patients. This is consistent with the larger number of males nationally participating in contact sports such as football, lacrosse and rugby. It can be noted that males occur more high velocity impact resulting in more severe concussions, as seen by the 83% of inpatient level of care concussions were males. Although, further studies comparing concussions and gender have shown that when looking at sports with similar rules, such as basketball and soccer, female athletes showed higher rates of concussions than males.

Concussions have also increased consistently for the past decade. Data gathered from the National Electronic Injury Surveillance Systems databases is shown below with marked increases from 2008-2012. This increasing trend may be due to the increased
teaching and awareness of parents and coaches to look for signs and symptoms. Athletes are also more aware of the risk of concussions and self-reporting symptoms more frequently. Despite the increase in reported concussions, severe head injuries such as fractures, subdural or epidural hematomas have not increased.

**Figure 1. Number of concussions cases per year, presenting to National Electronic Injury Surveillance Systems (NEISS) emergency departments from 2002-2012**

![Graph showing the number of concussions per year from 2002 to 2012](image_url)

**Pathophysiology**

Concussions are a very complex pathophysiologic process affecting the brain that is still not completely understood. Concussions occur when linear or rotational forces are transmitted to the brain from a direct impact to the skull or transitional forces from impact on other parts of the body. The acceleration and deceleration of the brain starts a complicated cascade of neurochemical and neurometabolic events. The stretching that
occurs during this movement of the neural tissue releases ions across previously regulated axons causing membrane defects. This change in membrane potentials causes a wide spread release of neurotransmitters, in particular excitatory amino acids such as glutamate. Free glutamate binds to ionic channels, such as N-methyl-d-aspartate, causing further depolarization and the release of calcium. Calcium overload is an important step in the neuro trauma cascade as it is responsible for changes to inner cellular membranes and dysfunction to mitochondrial processes\textsuperscript{10}. Impaired mitochondria result in the formation of reactive oxygen species (ROS). Build-up of ROS above the cells antioxidative defenses leads to irreversible changes to the cells membranes. To reestablish cell membrane balance, sodium/potassium pumps must work at maximum levels possible. This results in the need for increase ATP and oxygen. Due to the impairment of the mitochondria, cells are not able to maintain the ATP and oxygen levels needed to balance the cell membrane resulting in a decrease of ions moving across the cells membrane. Cells are then required to use glucose in a much less efficient attempt to maintain ATP levels\textsuperscript{11}. This comes at a time where metabolic levels of glucose are already diminished due to the eliciting trauma causing decrease blood flow to the areas that need the glucose the most. The changes in glucose levels as well as the impairment of cell membranes is thought to be the cause of cognitive and memory deficits\textsuperscript{2}.

Recent growths in technology and breakthroughs in research, have shown important advances at the molecular level of the brain. Important studies have shown that concussions are not simply milder forms of severe TBI but contain a separate pathology and repair in the brain. Due to the “silent” nature of the concussive symptoms, it was
previously difficult to study patients as individuals endorsed a variety of symptoms. Neuroimaging studies generally revealed no structural abnormalities but using functional magnetic resonance imaging, investigators have been able to show decreases in cortical blood flow to the prefronal cortex during the acute postconcussive phase when athletes were asked to perform memory tasks. Due to the recent advances in diffuse tensor imaging (DTI), investigators are now able to detect injuries of white matter and axons. DTI is MRI-based, which can examine microstructural integrity of white matter tracts. DTI does this by measurement of water molecule diffusion within the white matter thus providing information regarding the integrity of the tracts. Rotational forces to a fixed skull, are currently thought to the cause of damage to these white matter tracts. Damage to these tracts results in axonal injury and potentially damage to gray matter nuclei. These neural structural changes may be indicative of early chronic traumatic encephalopathy.

**Chronic Traumatic Encephalopathy**

Sports related chronic traumatic encephalopathy (CTE) consists of progressive cerebral neurological symptoms. This phenomenon is thought to be initiated and worsened by repetitive head traumas such as concussive and subconcussive impacts. CTE was first described by Dr. Martland in 1928, as “punch drunk”. He described boxers with symptoms such as confusions, slurred speech, tremors and behavioral changes. CTE since has been categorized into three stages of severity. Stage one, consists of emotional disturbances. Stage two, is classified by memory loss and early parkinsonian signs. Stage three is progression to dementia, full onset of Parkinson’s and cognitive
dysfunction. As much of the media attention has turned to CTE and NFL, more research on the pathophysiology has been initiated in the past decade looking at former NFL and college football players. CTE has been found to be a neurodegenerative tauopathy with the deposition of p-tau protein as a form of neurofibrillary tangles. This deposition leads to widespread dense collections in the temporal lobes as well as the white matter diffusely. Advance CTE has been shown to cause enlarged lateral and third ventricles with global atrophy of cerebral tissue. McKee et al, found a correlation between the severity of the pathology and duration of the athletic career, including duration from time of retirement until age of death. This data provided evidence supporting the more subconcussive and concussive impacts received, increases the risk and severity of CTE symptoms later in life.

Signs and symptoms

Concussions generally cause rapid onset of brief impairment of neurological function that in majority of cases resolves spontaneously. Concussions have a wide range of symptoms that generally occur during the acute phase, with in the first 28 days (Table 1). The vast majority of concussions (80-90%) resolve in the first week to ten days. Although, recent information shows recovery time may be longer in children and young adults. Unfortunately there is no way to predict what patients will have prolonged symptoms at this time.

Table 1. Signs and symptoms of a concussion

<table>
<thead>
<tr>
<th>Physical</th>
<th>Cognitive</th>
<th>Emotional</th>
<th>Sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>‘Foggy’</td>
<td>Irritable</td>
<td>Drowsiness</td>
</tr>
<tr>
<td>Symptom</td>
<td>Nausea</td>
<td>Slow comprehension</td>
<td>Depression</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------------------------</td>
<td>--------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Memory dysfunction</td>
<td>Mood Swings</td>
<td>Difficulty falling asleep</td>
</tr>
<tr>
<td>Balance disorders</td>
<td>Amnesia</td>
<td>Anxiety</td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>Confusion</td>
<td>Paranoid</td>
<td></td>
</tr>
<tr>
<td>Sensitivity to light/sound</td>
<td>Repetitive speaking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dazed</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Headache and dizziness are generally listed by patients as the two most common symptoms. Loss of consciousness occurs only 10% of the injuries and should not be used as a marker for diagnosis of concussions. LOC may be a predictor of the severity of the injury and warrant additional treatments. Along with recording current symptoms, it is important that previous concussion history be well documented as athletes may have worsening symptoms. If a concussion occurs while a patient is still recovering from a previous TBI, the patient may experience a phenomenon called second impact syndrome (SIS). SIS describes the loss of auto-regulation in the brain with cerebral edema being the result. SIS is generally noted on imaging of the brain with enlargement of cerebral blood vessels and marked increase in intracranial pressure. Although it is debated whether SIS is related to multiple concussions in close proximity, it is important to recognize as herniation and death can occur if not recognized quickly.
Although a large majority of athletes return to baseline a month after the initial injury, 10% of athletes have persistent symptoms. This is generally deemed postconcussion syndrome (PCS). Symptoms are generally vague and difficult diagnose. These symptoms are generally: fatigue, headache, dizziness, changes in memory or mental health issues such as depression or anxiety. More concerning is how PCS effects children. Studies have shown that PCS in children increases the risk of the patient developing depression by 3.3 fold. Even more concerning was seen in patients with family history of mental disorders as patients were seen to have an increase of depression by 4.8 fold. Although it is currently unsure why these increases exist, it is thought to be due to differences in the developing brain versus matured cerebral tissue including lower degree of myelination, decreased number of developed synapses and lower elasticity of the brain tissue.

Diagnosis

Evaluation of an athlete suspected to receive a concussion should occur immediately at the sporting event. Immediate intervention should be taken by medical personnel, in particular attention should be given to exclude cervical spine injuries. Player’s helmet or other essential piece of playing equipment should be held by administrative personnel to prevent player returning to play without being properly cleared. Once the player has been cleared from any acute bodily injury, concussive injury should be assessed using the Sideline Concussion Assessment Tool (SCAT) or other similar assessments. SCAT is currently being used by the NFL and will be discussed briefly for the purpose of this paper. NFL SCAT looks at LOC or changes in
mental status including amnesia or changes in neurological status. The test also looks at orientation of the player to time and place as well as specifics about the game the athlete was participating in. Memory and concentration are examined by word recall and number recollection. Balance as well as a symptom checklist are also included in the test. It should be noted that these test are for rapid concussion screening and should not replace medical providers clinical judgement or comprehensive testing by a trained neuropsychologist. Also of importance, symptoms may appear several hours following a concussive episode and patients should be evaluated with serial exams. For this reason, patients should never be left alone following a possible injury to monitor for deteriorating physical or mental status.

Athletes with concussions should be followed up in the emergency room or doctor’s office to provide a medical profession as a point of contact. Here providers should monitor for prolonged or worsening symptoms. If symptoms are worsening, neuroimaging may be required to examine severity of brain injury. Imaging is generally not recommended for concussions as majority of cases have little to no findings on scans.

Functional MRI or neuropsychological testing may be needed if symptoms are prolonged or patient has history of multiple concussions. Neuropsychological (NP) testing may be used to assist in return to play decisions and can be performed when an athlete is asymptomatic especially in high risk athletes. NP is just a small part of the return to play (RTP) guidelines and is not needed for all athletes. RTP guidelines are broken down to six stages, each stage requires 24 hours before the athlete can move to
the next stage. If symptoms return or worsen when a stage is increase, the athlete should return to the previous stage until symptoms have returned to baseline.³

**Table 2. Graduated return to play protocol**

<table>
<thead>
<tr>
<th>Rehabilitation stage</th>
<th>Functional limitations</th>
<th>Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Activity</td>
<td>Physical and cognitive rest, no exercise, schooling or tv</td>
<td>Recovery</td>
</tr>
<tr>
<td>Light aerobic exercise</td>
<td>Keep intensity below 70% max, no resistance training</td>
<td>Increase heart rate</td>
</tr>
<tr>
<td>Sport-specific exercise</td>
<td>Running or skating, no contact or head impacts</td>
<td>Add movement</td>
</tr>
<tr>
<td>Non-contact drills</td>
<td>Start resistance training, more complex drills</td>
<td>Exercise, coordination and cognitive load</td>
</tr>
<tr>
<td>Full contact practice</td>
<td>Participation in normal activities</td>
<td>Restore confidence, assessment of function</td>
</tr>
<tr>
<td>Return to play</td>
<td>Normal game play</td>
<td></td>
</tr>
</tbody>
</table>

These recommendations and protocols can be used for athletes down to 13 years old. Below 13, symptoms and recovery may differ from adults and require age appropriate assessments. Parents should be including in all evaluations done by the medical professional. A child SCAT is available for subjects ages 5-12. This tool is similar to the SCAT used in adults, but includes simpler vocabulary and tasks for memory recall. There is also a section for parent input and questions about school and
behavioral history. Children also are not able to return to play until the athlete has returned to school successfully. Due to the extended nature of symptoms in adolescent athletes, there may be longer duration of RTP protocol for each step, including longer cognitive rest prior to increasing the athlete’s functional status.

**Existing Research**

Due to concerns across mainstream media and the popularity of professional sports, research and recommendations concerning concussions are readily being released. Furthermore, increasing data is being studied concerning youth sports. The increasing data concerning head impacts and CTE has resulted in further discussions about the risks of youth playing contact sports and cognitive decline as they age. With millions of children participating in youth sports, these impact of concussions has become a growing public health problem.

Recently, Stamm et al. released a study discussing the retrospective correlation between the age of first exposure to football and cognitive impairment in adulthood. Stamm used two groups of former NFL players, those who played football prior to age 12 and those that started after age 12. To be included in the study, players had to have played at least two years in the NFL and 12 years of organized football. Players also had to endorse six months of complaints concerning cognitive, behavioral or mood symptoms. Players were excluded if they had any contraindications for MRI or lumbar puncture as well as previous diagnosis with CNS disease. Patients were tested using the a variety of neuropsychological measures such as the Wisconsin Care Sort Test and
Neuropsychological Assessment Battery List Learning Test. These raw scores were converted into T scores and analyzed using a paired-sample t test. Their results showed the age of football exposure group under 12 years old performed significantly lower when compared to the over 12 years old group in all NP testing. This significant difference demonstrated greater impairment of cognition, short and long term memory, and visual learning in the age under 12 group. This data is consistent with previous findings by Stamm et al. that showed players with exposure under age 12 were more likely to have depression, worse executive function and apathy than those with exposure after age 12. This data is thought to conclude that repetitive head impacts during important maturation of cerebral tissue may impact brain development resulting in earlier age related cognitive decline. This repetitive impacts around the time of peak development of the hippocampus region of the brain may affect the development of memory formation contributing to the significant decline seen in the this study. As discussed previously, a large majority of children have symptoms resolve in the first 28 days. Functional and cognitive impairments may not be seen during childhood but present in early adulthood when environmental demands increase. Although this study was able to correlate age of first impact with decreased cognitive function, the study did have its limitations. The participants associated with this study may have performed poorly do to media and other factors related to repetitive head impacts. Furthermore, due to pending law suits, players may have lowered their scores on purpose to influence their trial. Also, due to the recent increase in availability of youth sports, players in older generations may not have been able to participate in football until later in life. Lastly, due
to the retrospective nature of the study, researchers were only able to estimate total exposure during the course of their careers.\textsuperscript{17} With the recent use of accelerometers, future researchers will be able to closely monitor the amount of impacts a player receives.

Similar to this previous study, Dr. Guskiewicz et al. looked at the association between recurrent concussions and late life impairment. This study used two separate questionnaires to screen for cognitive impairment and symptoms. Due to the nature of the study, a large number of questionnaires were able to be sent to the National Football League Retired Player’s Association. In total, 2552 questionnaires were completed. The first questionnaire asked a variety of questions including medical conditions such as cardiovascular, neurological and musculoskeletal. It also included questions concerning the player’s concussion history and diagnosed mental health issues.\textsuperscript{18} A second questionnaire was sent to players over 50 years old, total of 1754 players. This questionnaire included questions concerning cognitive impairment, changes in daily living, possible AD or dementia. Results were compared using Chi-squared testing. The results showed the larger number of concussions reported, the lower the player scored on the mental components of the test with the mean score for 0 concussions being 54.35 and the mean score for 3+ concussions being 50.31. These results were significant with P<0.001. Players with recurrent concussions also were shown to have earlier diagnosis of possible AD and dementia when compared to the general public.\textsuperscript{18} Although Guskiewicz et al. were able to show a correlation between concussions and early onset disease, there was no significant data that showed association between previous concussions and lifetime onset of the disease.
Although this data did not show an association with lifelong risk of AD, they were able to show that retired players with 3+ concussions were five times more likely than those with no concussions to be diagnosed with moderate cognitive impairment. These findings suggest and correlate with the findings of Stamm et al. The increase in head impacts and concussions may result in reductions of brain development and reduce cerebral repair factors resulting in memory and cognitive impairment. This study was also without its limitations. The retrospective aspect of the study makes it hard to determine in players completely recall each concussion. The self-reporting nature of the questionnaires causes uncertainty to how well the players are endorsing symptoms of cognitive impairment or memory changes. Although there are limitations, the data still suggest that increased exposure to concussions may cause increase cognitive decline and earlier diagnosis with AD or dementia.

Due to these factors involving possible delay or impairment of cerebral maturation due to injury, Dr. Moore et al. looked at the influence of concussions on attention and executive control in children. A total of 30 participants were selected from central Illinois youth athletic associations. All participants were between the ages of eight and ten. Each participant in the case group had their concussion diagnosed by the same Central Illinois healthcare system. Of the 15 players with concussions, eight had LOC but no one required further surgical intervention. To be included in the study, all participants had no history of special education needs or behavior/neurological disorders. Participants in the case group could only have been diagnosed with one concussion. Once included in the study, participants were matched with age, sex, pubertal timing, IQ, ADHD
symptoms, BMI and social support. These matches were performed due to the influence they have on brain and cognitive development and the benefits they provide on recovery. Participants were then tested using a variety of physical and cognitive tests. Researchers examined participants’ attention and working memory, behavioral inhibition, mental flexibility and reaction times. Participants were also monitored using EEG during tasks. Results showed that children with history of concussion showed an overall decrease in response accuracy and discriminability during tasks. Most concerning, children injured earlier in life showed the largest deficits. Furthermore, children injured earlier in life showed greatest deficits when looking at global working memory. Lastly, children in the concussion group showed greater deficits in impulse control and inhibition. This data may further suggest that concussions affect the hippocampus and frontal lobe areas of the brain resulting in memory impairment and personality changes. These changes may not be notable during childhood but may present later in life following full maturation and increased environmental influences. This data is consistent with findings from previous studies from Moore et al. concerning sensory and visual processing. In this study 38 adults ages 20-29 were recruited from University of Illinois club or recreational athletics. All participants with concussions had been diagnosed prior to age 18. Participants underwent EEG and Visual Evoked Potential testing. Their findings showed that participants who were diagnosed with a concussion prior to age 18 had lower amplitudes of visual evoked potentials. This data suggest that concussions occurring early in life may have negative consequences on visual processing years following impact. These findings suggest that concussions may not only effect higher
executive function but may also effect vision and perceptual sensory function. Also, since lower sensory function such as vison and perception contribute to higher function, these decreases in visual function may compound higher executive task such as memory and verbal reasoning.

Although these studies showed many strengths with the extensive testing and matching, there are still many limitations. The small sample size makes it difficult to make general statements concerning the results and also reduces the amount of variable that are able to be observed. Furthermore, parents who agreed to testing may have had concerns with their child’s behavior or education performance prior to testing. This may have swayed the data to be more concerning than actually anticipated across a wide range of athletes. Longitudinal studies will be able to pin point greater changes from baseline by using baseline testing and reducing self-reported symptoms years following diagnosis.

Recent studies on imaging of cortical structures for chronic mTBIs by List et al, have shown that recurrent concussions decreases cortical thickness. These findings were consistent with decreased cognitive scores and decreased verbal efficiency \(^{20}\). Although the decreased scores on cognitive testing was small, the scores were consistently low across athletes with multiple concussions. Multiple concussions were linked to a dose-dependent thinning of the temporal lobe when compared to subjects without history of TBI. The lower thickness is associated with lower verbal understanding and may be linked to the first signs of Alzheimer’s disease (AD)\(^{21}\). Furthermore, mTBIs were shown to also decrease the thickness of the cortex in the entorhinal area. The entorhinal cortex function is primarily for memory generation and recall, making it an important area in the
connection to AD. Since thinning of the entorhinal cortex is associated with severity of AD, concussion caused entorhinal thinning may increase the risks of athletes developing AD earlier in life. Studies have shown that the severity of head injury is may be correlated to the risk of AD. Guo et al, showed that the risk of AD associated with head injury with loss of consciousness (LOC) was almost double that of patients who experienced head injury without LOC. Additionally the use of functional MRI has shown that patients with multiple TBIs have less efficient recruitment of neural regions during memory tasks, resulting in delayed or impaired responses. This has been seen to be true even with patients that show no significant behavioral or mental defects.

Although little information remains on the acute impact of multiple concussions on younger subjects, inflammation and changes in neurometabolism may set forth a cascade of effects that led to changes in cortical structure resulting in detrimental effects later in life.

The ability to identify patients who may be susceptible to neurocognitive decreases following concussions is also an important way to prevent future injuries as well as tailor treatment plans to each individual patient. Dr. Thomas et al. looked at the use of ImPACT testing in the emergency room following the diagnosis of a concussion in patients ages 11-17. Testing was performed within 12 hours of the initial injury and again three to ten days later. Following symptom reporting was performed via telephone calls.

**Table 3 ImPACT test features.**

<table>
<thead>
<tr>
<th>Module</th>
<th>Methods</th>
<th>Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Word Discrimination</td>
<td>-12 target words are given and must be identified from a series of 24 words.</td>
<td>Verbal memory</td>
</tr>
</tbody>
</table>
Follow up testing showed that patients had significant reduction in ImPACT scores with majority of patients below the 50th percentile. Follow up telephone questioning also showed that 85% of participants showed at least one symptom three months following the initial impact with 20% of patients still not returning to normal activity one month following concussion. Although this study did not find a correlation between ImPACT scores and duration of symptoms or return to play, it did so that testing can be used in the ED to monitor the severity of symptoms and cognitive decline. These
findings can help medical providers tailor therapy and rest to the severity of changes. Since ImPACT testing as shown cognitive decline even when patient deny symptoms, it may be a helpful marker for assisting return to play criteria especially when baseline testing have been performed prior to injury.23

Although these studies continue to suggest the impact of concussions on the development and later in life outcomes of athletes with concussions, there is still little information about how many concussion or the severity influences these outcomes. Due to the recent concern of CTE and changes in development, longitudinal studies are needed to further research and control for variable concerning these outcomes. Also the changes in player’s safety, including tackling rule changes, the use of increase safety equipment and the increase vigilance to concussion symptoms may be already changing the outcomes seen in previous generations of athletes. Future longitudinal studies would also be able to show the impact of these changes that may influence the future of not only football but all contact sports.
METHODS

Study design

For this study, researchers will use a longitudinal study to follow youth football players over the course of their development, from ages 10 to 25. Participants will be monitored for cognitive function changes over the duration of their maturation.

Study population and sampling

Participants for this study will including football players at the age of 10 years old in the state of Massachusetts. Due to the low number of female participants in youth football, only male participants will be included to reduce the amount of variables in the study.

Table 4. Inclusion and Exclusion criteria.

<table>
<thead>
<tr>
<th>Case Group</th>
<th>Control Group</th>
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<tbody>
<tr>
<td>Inclusion</td>
<td>Exclusion</td>
</tr>
<tr>
<td>Age ten, Male</td>
<td>Female</td>
</tr>
<tr>
<td>First year participants in Pee Wee football</td>
<td>Previous history of behavioral, psychiatric or neurologic condition</td>
</tr>
<tr>
<td></td>
<td>Previous head trauma</td>
</tr>
<tr>
<td></td>
<td>Participation in other contact sports</td>
</tr>
<tr>
<td>-Age ten, Male</td>
<td>-Age ten, Male</td>
</tr>
<tr>
<td>-No history of participation in contact sports</td>
<td>-Female</td>
</tr>
<tr>
<td>-Previous history of behavioral, psychiatric or neurologic condition</td>
<td>Previous participation in contact sports</td>
</tr>
<tr>
<td>-Previous head trauma</td>
<td>-Previous head trauma</td>
</tr>
<tr>
<td></td>
<td>-History of behavioral psychiatric or neurologic condition</td>
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</table>

Using the State of Massachusetts will allow for a wide sample population ranging from all races, cognitive function and social-economic status. Assuming a cognitive decline may be noted of 4% from the unexposed group with a two time greater risk in the exposed group, a sample size of 550 would be needed for each group. Assuming 40% attrition rate over the course of the study, a total sample size of 1540 athletes would be
needed to obtain a 95% confidence level and 80% power. This large of a sample size will also allow for inclusion of athletes that are able to continue to play football at the collegiate level. This will allow for analysis of data for athletes that continue to play contact sports into their twenties versus participants that stop at a younger age.

**Recruitment**

Participants will be recruited from Pop Warner and Pee Wee football in Massachusetts. Participants will be chosen from each region of Massachusetts to include all races, social economic status and variety of school systems. Control group participants will be recruited from local school districts and family practice physician offices. Question and answer sessions will be set up with school districts to answer any concerns from parents. Teaching sessions will also be set up for parents and participants about understanding concussions as well as the prevention and treatment process. At this time, agreeable participants will be provided with information regarding the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT). Participants will be instructed on the benefits of baseline testing and as well as logistics concerning taking the test.

**Study Procedure**

Participants at age 10 will be placed in two separate groups depending on their participation in youth football or if they are not a part of contact sports. Participants will complete baseline testing using ImPACT as part of a standard clinic and pre-exposure visit. Questionnaires will be completed by the participant and the caregiver of the child (parent, guardian, etc.). When creating the questionnaires, it will be important to adjust
for younger children’s less developed vocabulary and difficulty discerning different levels of severity of symptoms\textsuperscript{24}.

Follow up testing will occur every year to maintain the relationship with the participants as well as document any changes in development over that time. Conussions, if any, will be recorded during each visit for the previous year. Changes in participation in youth football will also be documented. Participants that drop out of football will continue to be followed throughout the study. Control group participants that join football or a contact sport at any point during the study will be censored. Only data obtained prior to joining contact sports will be used.

**Study variables and timeline**

Participation in contact sports will be used as the primary variable. A change in ImPACT scores by 10\% will be deemed significant. Subgroups can be broken down to including participants in contacts sports at the Pee Wee level only, Pee Wee and high school level or Pee Wee, high school and college. Age ten will be the starting point for this study. This age was selected based on research that shows key neurodevelopment occurs at this time. Age 25 will be selected as the completion of this study. Age 25 also allows for completion of data as athletes may continue to play contact sports throughout their college years. Secondary variables also include duration of participation, position the athlete plays and socioeconomic factors.

**Data collection**

Data will be collected by researchers on a yearly basis. Participants will be scheduled for testing times and can be performed at the participant’s house, school and
researchers office. Baseline data will be collected at age ten prior to the onset of youth football for clinical group and at age 10 for control group. The control and clinical groups will be followed yearly until the exclusion criteria is met or the participant reaches age 25.

**Data analysis**

All data will be analyzed as it is collected each year. Questionnaire responses will be used as a 5 point Likert scale, 5 being the most severe symptoms and 1 being no symptoms. Parent and participant data will be analyzed separately. This data will be used to correlate subjective symptomatic results with ImPACT data. ImPACT data will also be analyzed yearly. Scoring will be based on ImPACT guidelines. Changes of 10% will be used as significant as found in previous research. Data will be analyzed using a chi-squared test to compare if the observed changes would be different than expected. Risk ratio calculations will be calculated using changes in ImPACT results and exposure to concussions. The model can furthermore be adjusted to compare subgroups of duration of play, education, BMI, and age of puberty onset.

**Timeline and resources**

<table>
<thead>
<tr>
<th>Fall 2016</th>
<th>• Submit for IRB approval</th>
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<tbody>
<tr>
<td></td>
<td>• Obtain approval from youth football and Massachusetts Public School</td>
</tr>
<tr>
<td>Winter-Fall 2017</td>
<td>• Recruit participants prior to the start of the youth football</td>
</tr>
</tbody>
</table>
The study will require multiple resources throughout its completion. A primary investigator will be used for oversight of the testing and data collection. Multiple co-investigators will be required to allow for multiple testing areas though out the state of Massachusetts. These investigators will be split up into regions to reduce the cost of travel. A statistician who is familiar with SAS and QRS NVivo will be required yearly to help analyze data. Lastly for personnel, a study coordinator will be required to help manage and schedule testing for participants throughout the course of the study.

Equipment needed for this study will include multiple laptop computers for ImPACT testing. Central office space will be required to maintain the data and analysis throughout the study. Testing done outside of the central office can be completed at schools, medical facilities or participants housing to reduce the cost of multiple office spaces.
Institutional Review Board

This study will be submitted for full IRB approval. Due to the nature of the participants being under the age of 18 and minors at the start of the study, there is greater risk and warrants full board approval.

CONCLUSION

Discussion

This study would help bridge a gap in research concerning the effects of concussions on adolescents participating in football. The longitudinal study design would allow for more control of variables as well as up to date information concerning the player’s medical conditions and other changes with mental or behavioral function. The use of the longitudinal design would also allow for multiple subgroups to further match participants. This would allow for medical providers to document and follow the athlete’s current condition without relying on data provided by the patient years following the concussion. Symptoms will also be documented in real time over the course of the study to allow researchers to follow how symptoms resolve and reoccur following repetitive concussions. Another benefit to a longitudinal study will allow for testing of the athletes throughout the course of their development. This may also provide important information concerning head impacts at different stages of maturation. These results could be used to change contact rules in sports as well as adjust how athletes are managed with return to play rules.
Furthermore, due to the large number of participants, a variety of BMI, socioeconomic status, education level and race would be included. This large sample size would make results more generalizable across a wide population of youth athletes participating in football.

Although this study would provide valuable information when looking at concussion and the developing brain, it is not without limitations. First, the study would only be following athletes participating in football. Data would not be collected from other high contact sports such as soccer, hockey and lacrosse. Furthermore, only male athletes would be followed. This would limit the use of the data on the female population which may be more susceptible to concussions. Lastly, this study would only be using the ImPACT testing for use of cognitive function. Although ImPACT has been used and studied extensively, it still may not observe all related cognitive changes seen over a chronic period of time.

Summary

Following the review of the current literature, it is clear that the study of concussions is just beginning. New technology and better understanding of the pathophysiology of concussions will allow for more tailored treatments and better safety equipment for future generations. Current studies continue to show that head impacts lead to higher risk of mental and behavior problems later in life. Cognitive changes lead to higher mortality and morbidity and cause increase burden on loved ones. These changes also impact society by causing billions of dollars in medical expenses each year. 25 By understanding what repetitive head impacts have on future life condition, would allow medical and
athletic personal to treat and prevent these diseases from occurring to a vast range of athletes. Longitudinal studies such as this would allow for more detailed research into concussions received by adolescents and how it may impact their development. With further demand for more understanding of mental and behavioral conditions, research such as this may allow for better understanding of the causes of behavioral changes seen in retired athletes.

Using conclusions found from this study could greatly impact society today. With millions of youth athletes participating in youth sports leagues yearly, it may have a vast impact upon medical, safety and professional sports. Changes could be seen pertaining to rules at all levels of competition as well as reduction in amount of contact allowed. Medical treatment plans could be adjusted and return to play may be prolonged in cognitive changes are seen. With billions of dollars in revenues seen from football every year, the impact of further studies into concussion could have vast and important effects in both football and our society today.
## LIST OF JOURNAL ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>Am Acad Neurol</td>
<td>American Academy of Neurology</td>
</tr>
<tr>
<td>Arch Clin Neuropsychol</td>
<td>Archives of Clinical Neuropsychology</td>
</tr>
<tr>
<td>Clin Sports Med</td>
<td>Clinical Journal of Sports Medicine</td>
</tr>
<tr>
<td>Front Hum Neurosci</td>
<td>Frontiers in Human Neuroscience</td>
</tr>
<tr>
<td>J Athl Train</td>
<td>Journal of Athletic Training</td>
</tr>
<tr>
<td>J Cereb Blood Flow Metab</td>
<td>Journal of Cerebral Blood Flow and Metabolism</td>
</tr>
<tr>
<td>J Neurotrauma</td>
<td>Journal of Neurotrauma</td>
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<tr>
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<td>Neurosurgical Focus</td>
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<tr>
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<td>Paediatrics and Child Health</td>
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<tr>
<td>PLOS ONE</td>
<td>Public Library of Science</td>
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<tr>
<td>PM&amp;R</td>
<td>Physical Medicine and Rehabilitation</td>
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</tbody>
</table>
REFERENCES


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EDUCATION

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Graduated with honors

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Intra-operative Neuromonitoring Tech
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• CNIM Certified
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• Certified in SSEPs, EMG, TcMEPs, CE, ABRs and Cranial Nerves
• Senior Tech, Chicago North

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Archer Sign Company

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Industrial part fabrication
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• Certification by the National Commission on Certification of Physician Assistants- Pending
• Advanced Cardiac Life Support- February 2015
• Certification of Neuro Intraoperative Monitoring- August 2010

Presentations

• Doerr, M., Sepsis, VA Healthcare Brockton Community Living Center, Brockton Massachusetts, January 2016
• Doerr, M., Insulinoma, Boston University School of Medicine Physician Assistant Program, Boston, Massachusetts, April 2016
• Doerr, M., Avascular Necrosis, Boston University School of Medicine Physician Assistant Program, Boston, Massachusetts, June 2016
• Doerr, M., Ultrasound Use in Trauma Setting, VA Healthcare Brockton Community Living Center, Brockton Massachusetts, January 2016