Written Testimony

Ann C. McKee, M.D.

Professor of Neurology and Pathology

Boston University School of Medicine

Director of the VISN-1 Neuropathology Laboratory for the New England Veterans Affairs Medical Centers

Director of the Brain Banks for the Boston University Alzheimer's Disease Center, Framingham Heart Study, and Centenarian Study

Co-Director, Center for the Study of Traumatic Encephalopathy

Hearing before the Senate Committee on Commerce, Science & Transportation

October 19, 2011

Mr. Chairman and Members of the Committee:

Thank you for the invitation to testify today on sports concussions and their consequences. My name is Dr. Ann McKee. I am a Professor of Neurology and Pathology at Boston University School of Medicine and I am the Director of the Neuropathology Laboratory for the New England Veterans Affairs Medical Centers at the Boston VA Medical Center. I also direct the Brain Banks for the Boston University Alzheimer's Disease Center, the Framingham Heart Study, and the Centenarian Study, and I am a co-director for the Center for the Study of Traumatic Encephalopathy at Boston University. My testimony today reflects my professional opinion; I am not speaking officially on behalf of the Department of Veterans Affairs.

I received my medical degree in 1979, and I am board certified in both Neurology and Neuropathology. I have broad experience in neuropathology of neurological disease and have written extensively on the neuropathology of many neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, Frontotemporal Dementia and Traumatic Brain Injury. For the past 25 years, I have been studying the brains of individuals after death and correlating the pathological findings to the patient's clinical symptoms during life. For the past 9 years I have been specifically analyzing the effects of repetitive mild traumatic brain injury or repetitive concussion on the brain.

A traumatic brain injury (TBI) is caused by a blow, a jolt to the head or a penetrating head injury that disrupts the function of the brain. A TBI may range from mild - with a brief change in mental status - to severe, with an extended period of unconsciousness or amnesia after injury. Eighty percent of all TBI is mild, approximately 10% is moderate, and approximately 10% is severe. What we are primarily concerned with today is repetitive mild TBI (mTBI) or concussion; the

terms concussion and mild TBI are interchangeable. Mild TBI and concussion are temporary states of neurological dysfunction resulting from acceleration, deceleration, lateral and rotational forces on the brain. Subconcussion is caused by the same acceleration-deceleration-rotational forces but the forces are milder and no symptoms are produced. In all these conditions, the brain appears macroscopically normal after the injury and there is no detectable damage on routine neuroimaging, including CT scan or MRI, which is why concussion and subconcussive injury are sometimes considered "invisible" brain injuries. However, these acceleration-deceleration-rotational forces cause the brain to move rapidly within the skull and the brain, which is firm, but gelatinous, is stretched and deformed by these forces. As the brain as a whole is deformed, there is also stretch and strain of the individual nerve cells and supporting cells within the brain. The brain abnormalities associated with concussion and subconcussion occur at the microscopic, cellular, molecular and metabolic levels. There is mild, but widespread injury to axons, the long, slender projections of a nerve cell that conduct electrical impulses away from the nerve cell and contact other nerve cells. The nerve cell and axonal injury most often completely resolve with rest. Indeed, most individuals recover completely from a single mTBI or concussion within weeks to months, but in some individuals (fewer than 10%), post-concussive symptoms can last for months to years, especially in situations where an athlete is not properly treated after a concussion. If an athlete returns to play before symptoms resolve, the athlete also risks a rare but sometimes fatal event known as second impact syndrome (SIS). In addition, repetitive concussion or repetitive subconcussion can trigger a progressive deterioration of the brain called Chronic Traumatic Encephalopathy (CTE) (McKee 2009, McKee 2010, Gavett 2010, Daneshvar 2011, Gavett 2011).

CTE is a progressive neurodegeneration triggered by repetitive concussion and subconcussion that evolves slowly over decades and usually does not become apparent until many years later.

Although the exact relationship between concussion, subconcussion and CTE is not entirely clear, most likely repetitive concussive and subconcussive injury superimposed on unresolved nerve cell and axonal injury initiates a series of metabolic, ionic, membrane, and cytoskeletal disturbances that triggers the pathological cascade that leads to CTE. This is the reason why concussion awareness is so critical and why proper diagnosis and management of concussion, allowing the brain to completely rest and recover after an injury, is so important in youth sports and all other activities that result in mTBI.

There is also evidence that the youth or immature brain may be more susceptible to concussive injuries than the mature adult brain. The brain continues to develop and mature, laying down myelinated fiber tracts, until the mid-twenties. Children and young adults recover more slowly from a concussion than adults. Youth athletes are also more at risk for concussion due to their disproportionately large head size compared to body size and the weakness of their neck musculature. Further evidence of the enhanced susceptibility of young athletes to mTBI is second-impact syndrome (SIS), an entity that has only been reported in athletes 24 years and younger, and the vast majority of the SIS cases in the literature have involved athletes under the age of 18.

SIS occurs when a young athlete sustains an initial head injury and then suffers a second head injury before the symptoms associated with the first impact have cleared (Cantu and Gean 2010). Typically, the athlete suffers post-concussion symptoms after the first head injury, which may include headache; dizziness; visual, motor, or sensory changes; confusion and memory problems. Before these symptoms resolve, which may take days or weeks, the athlete returns to competition and receives a second blow to the head. The second blow may be remarkably minor. The affected athlete may appear stunned, usually does not experience loss of consciousness but in the next few seconds to several minutes, the athlete, who is conscious yet stunned, precipitously collapses to the ground, semicomatose. The outcome is often fatal or

associated with severe permanent disability. The pathophysiology of the SIS is generally believed to be caused by a loss of autoregulation of the cerebrovasculature. This dysautoregulation leads to precipitous brain swelling, high intracranial pressure, brain herniation and often, death. The adolescent or youth brain does not autoregulate well and is more susceptible to poor outcomes following mTBI (Chaiwat 2009).

In 2008, we created the Center for the Study of Traumatic Encephalopathy (CSTE) with the goal of studying the long-term effects of sports-related mTBI and CTE. We initiated a brain donation registry, a clinical registry of amateur and professional athletes, and the CSTE Brain Bank at the Bedford VA. The purpose of the VA CSTE Brain Bank is to study the effects of repetitive mTBI (repetitive concussion and subconcussion) by neuropathologically examining brains donated by deceased athletes and other individuals with a history of repetitive mTBI.

CTE was first reported in 1928 by Harrison Martland, a New Jersey pathologist and medical examiner, who described the clinical spectrum of abnormalities found in “nearly one half of the fighters who have stayed in the game long enough" (McKee 2009, Gavett 2011). Boxers exhibiting cognitive, behavioral, or motor abnormalities were well known within the community and were referred to by various terms, such as “punch drunk,” “goofy,” and “slug-nutty”, and later by the more formal term "dementia pugilistica". By the 1970s, a sufficient number of boxers with dementia pugilistica had been studied pathologically to support the conclusion that this distinct neurodegeneration was a consequence of repeated mTBI and was not restricted to boxers, and the term "chronic traumatic encephalopathy" or CTE, became most widely used. Over the last few decades, clinical and neuropathologic evidence of CTE has emerged in association with various sports, including American football, professional wrestling, professional hockey, and soccer, as well as other activities associated with repetitive mild head trauma, such as physical abuse, epileptic seizures, head banging and military service. Although the incidence and prevalence of CTE is currently unclear, it most likely varies by sport, position, duration of

exposure, and age at the time of initial or subsequent head trauma, and additional variables, such as genetic predisposition.

In 2009, I reviewed the world's literature on neuropathologically-verified CTE and found 51 cases of CTE including 3 cases of our own from BU and the Bedford VA (McKee 2009). Over the past 3 1/2 years, the brains and spinal cords of 97 athletes and military veterans who experienced mTBI or concussion have been donated to the VA CSTE Brain Bank. We have found CTE in 58 individuals, more than doubling the history of the world's experience combined. We have neuropathologically diagnosed CTE in 40 football players, at all levels of play, professional, college and high school, 5 hockey players, and 15 military veterans and are currently preparing a manuscript for submission describing our experience.

The onset of CTE is often in midlife, usually after athletes have retired from their sport. The early manifestations of CTE affect behavior and personality; in particular, individuals with neuropathologically documented CTE have been described as being more irritable, angry, or aggressive or as having a shorter fuse. There are mood changes, usually of depression, and increased suicidality, drug and alcohol abuse, and paranoia may be present. These changes are usually followed by short-term memory loss and executive dysfunction. Later in the disease, increasing cognitive impairment, movement disorders (e.g., parkinsonism), and speech disorders may emerge.

Macroscopic pathological changes found in CTE include an anterior cavum septum pellucidum and posterior septal fenestrations. These changes are likely caused by the force of the head impact being transmitted through the fluid ventricular system, thereby affecting the integrity of the intervening tissue. Enlargement of the lateral and third ventricles is also commonly seen in CTE with the third ventricle disproportionately widened. In advanced cases, there is also

atrophy of the frontal and temporal cortices and medial temporal lobe, thinning of the hypothalamic floor, shrinkage of the mammillary bodies, pallor of the substantia nigra, and hippocampal sclerosis.

Microscopically, CTE is characterized by an abundance of neurofibrillary tangles (NFTs), neuropil threads, and glial tangles within the brain, composed of hyperphosphorylated tau protein. CTE is distinguished from other neurodegenerations associated with build up of tau protein, such as Alzheimer's disease, by several unique features. First, the distribution of tau pathology in CTE is strikingly perivascular and most dense at the depths of cortical sulci, especially in early stages of the disease. The tau pathology in CTE is also extremely irregular and superficial, largely confined to foci in the frontal, temporal, and insular cortices. With increasing severity the tau pathology spreads to involve the limbic cortices, subcortical nuclei and brainstem.

Recently, in addition to severe tau neurofibrillary pathology, we have found that there is a widespread TDP-43 proteinopathy in more than 80% of their cases of CTE. Ten percent of athletes with CTE and a florid TDP-43 proteinopathy also develop a motor neuron disease similar to Amyotrophic Lateral Sclerosis (McKee 2010). The deposition of both tau and TDP-43 as aggregated phosphorylated proteins associated with neurodegeneration in CTE suggests that repetitive mTBI or repetitive axonal injury provokes the pathologic accumulation of both proteins.

Case studies

Cognitively normal individuals

Under normal circumstances, phosphorylated tau protein, is found only in very limited quantities in the brains of cognitively normal people. I have examined over 70 brains of cognitively intact

individuals ranging in age from 18-103 years using the identical techniques that I use in studying the athlete brains. Basically, unless the individual is in the preclinical stages of a neurodegenerative disease, there is very little "normal" build up of phosphorylated tau protein in the brain and then only in restricted regions of individuals aged 70 years or older (Figure 1).

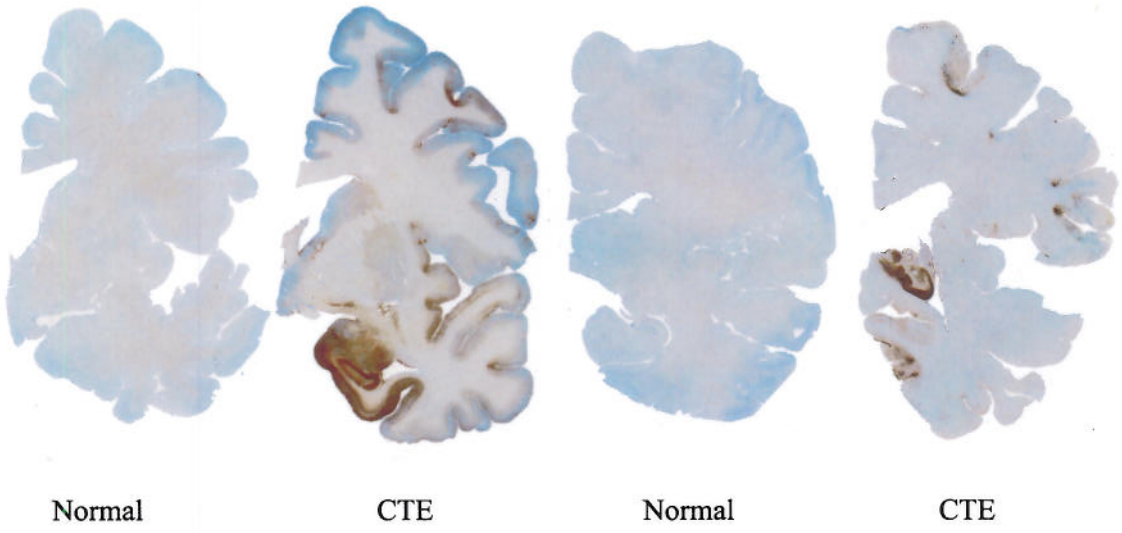


Figure 1. Coronal sections of brain from a 65-year-old cognitively normal individual without a history of mild TBI compared to the changes found in a 66-year-old former NFL player with CTE. The brain sections have been immunostained for phosphorylated tau protein, which appears as a dark brown color when the slides are viewed with the naked eye. The normal brain does not contain any appreciable amounts of phosphorylated tau protein, however there are substantial deposits of tau protein in many regions of the brain in the individual with CTE.

Case 1. Former professional boxer

In January of 2003, as part of my work with the Boston University Alzheimer's Disease Center and the Bedford VA, I examined the brain of a man who died at the age of 72 after 15 years of

severe dementia requiring institutionalization. The man had been a world champion boxer and had been clinically diagnosed with Alzheimer's disease beginning at the age of 58. However, when I looked at his brain on post-mortem examination, I found that there was absolutely no evidence of Alzheimer's disease; there was no evidence of *beta amyloid*, a protein that accumulates in the brain in people with Alzheimer's disease and is thought by many to be the cause of Alzheimer's disease. Instead, the brain of this world champion boxer showed a massive build-up of phosphorylated tau protein as NFTs and glial tangles throughout his brain. The neurofibrillary and glial tangles were distributed in a unique pattern that is diagnostic of CTE; this pattern not found in any other neurodegenerative condition. When viewed microscopically it was clear that many individual nerve cells of the boxer contained NFTs, in fact they were found in nearly every nerve cell and there were almost no normal appearing cells. In CTE, tau protein builds up in individual nerve cells and prevents them from making normal connections with other nerve cells, eventually killing the cells. In this man's brain, there were massive numbers of NFTs and glial tangles, so many in fact that you could see the abnormalities on the glass slides without the use of a microscope (Figure 2). This individual, a former professional boxer, had been clinically diagnosed with Alzheimer's disease during life, but the disease that actually caused his tragic 15 year decline in intellect and eventual hospitalization for severe dementia was CTE, a disorder that would have been entirely prevented if he hadn't suffered repeated head injury in his younger years as a boxer.

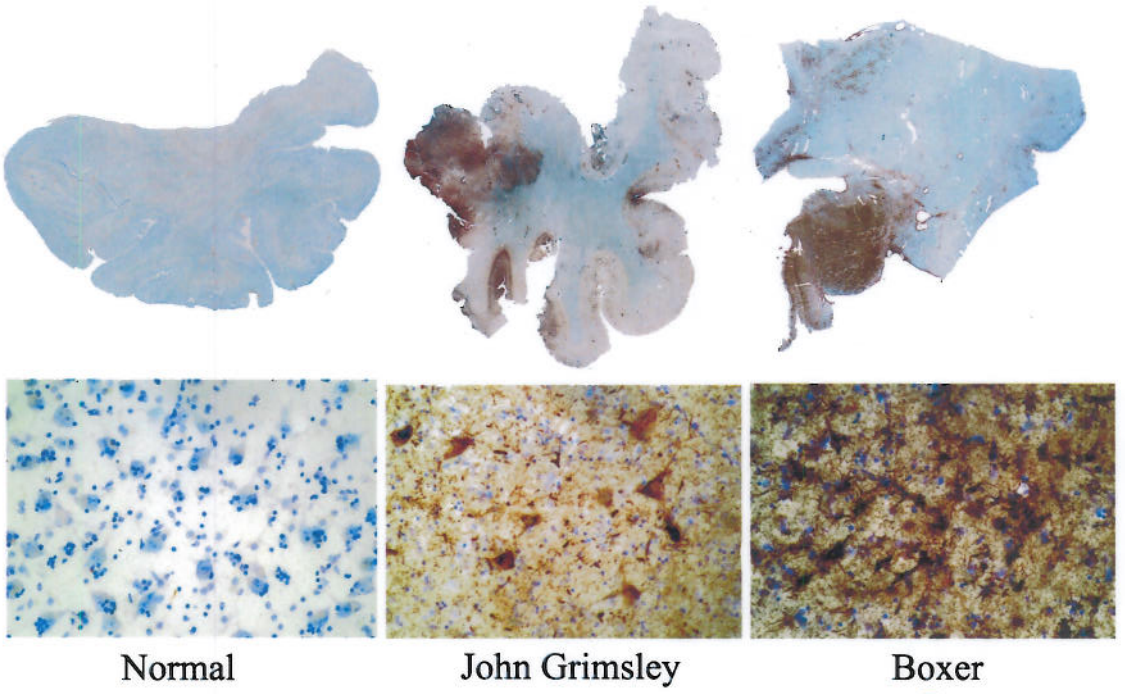


Figure 2.

Left panel, top and bottom: coronal section of brain from a normal control showing the absence phosphorylated tau protein (dark brown). The bottom section is a microscopic view of a normal brain showing intact nerve cells and support cells. Middle panel, John Grimsley, showing marked deposition of tau protein in the amygdala and temporal cortex (top) and nerve cells filled with abnormal tau protein (bottom). The sections on the right are from a 72 year old professional boxer who died with advanced CTE. The top section shows dense deposition of abnormal tau protein in the amygdala and the bottom section shows a microscopic view of the dense accumulation of tau in nerve cells and support cells.

Case 2. John Grimsley, former linebacker Houston Oilers

John Grimsley, a former linebacker for the Houston Oilers died of an accidental gunshot wound while cleaning his gun at the age of 45. According to his wife, he was concussed 3 times during his college football years, and at least 8 times during his NFL career, however, only one

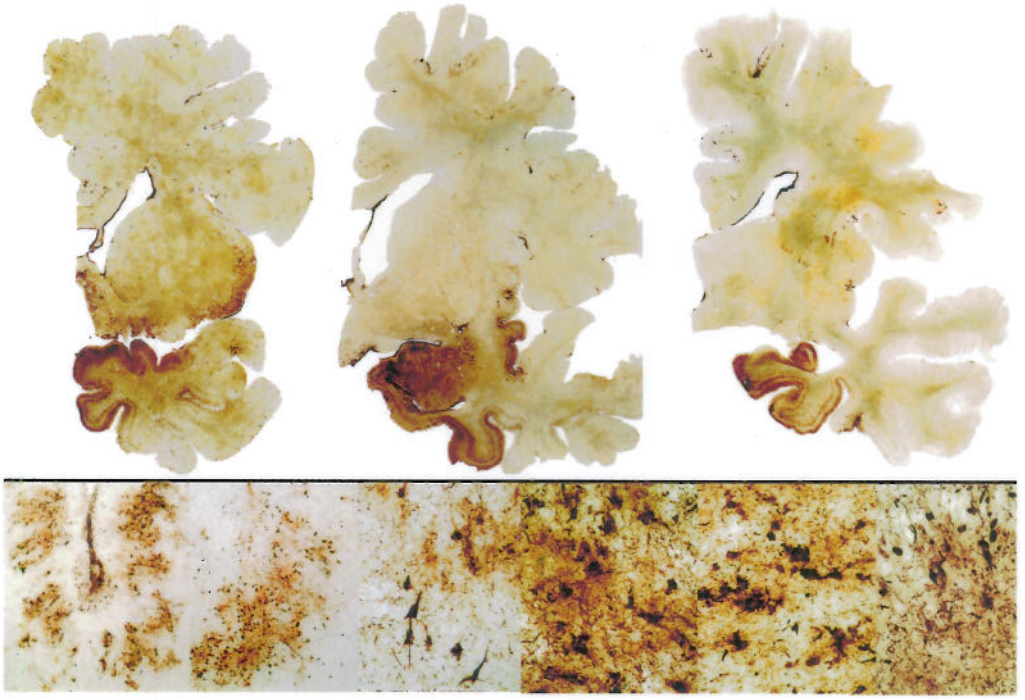
"cerebral concussion" was medically confirmed. He was never formally diagnosed with post-concussion syndrome and never sought medical attention for residual cognitive and behavioral difficulties. There was no history of ever losing consciousness for more than a few seconds and he never required being carried off the field or hospitalization. He never took any performance-enhancing drugs or used illicit drugs. He was a nonsmoker and there was no known family history of dementia. According to his wife and close friends, he began showing changes in his behavior and cognitive decline at age 40. He developed difficulties in short-term memory, attention, concentration, organization, planning, problem solving, judgment, and the ability to juggle more than one task at a time. For example, he would ask the same questions repeatedly over the course of the day and he would ask to rent a movie that he had already seen. He had difficulty assembling his tax records, shopping alone, and understanding television. His symptoms gradually progressed and became quite severe by the end of his life. He also developed a "shorter and shorter fuse" and would become angry and verbally aggressive over seemingly trivial issues. When I first looked at his brain, it showed the exact same pattern of changes that I had found in the brains of boxers with CTE. There were large numbers of tau containing neurofibrillary tangles throughout all parts of the brain and there was absolutely no evidence of beta amyloid protein or Alzheimer's disease. The brain of this 45 year old husband and father, at the prime of his life, showed profound neurofibrillary degeneration, changes of CTE that were identical in nature to the changes I found in the brains of the boxers, but were now found in a football linebacker some 30 years younger. In John Grimsley's brain, there were striking changes in regions of the brain controlling personality and behavior, such as the frontal lobes, profound changes in the areas controlling impulsivity and rage behavior such as the amygdala, and severe changes in anatomic structures that are responsible for memory, such as the hippocampus, mammillary bodies and thalamus. In Figure 2, the brain of John Grimsley is seen in the middle; in the top middle panel, you can see severe tau deposition in the frontal lobe and microscopically; in the bottom middle panel, you can see numerous nerve cells containing

tau and NFTs. In a normal 45 year old, absolutely none of these changes would be found. Indeed these changes would not be found in a normal 65 year old, 85 year old or 100 year old.

Case 3. Louis Creekmur, former offensive lineman Detroit Lions

Louis Creekmur was a former offensive lineman for the Detroit Lions and eight-time Pro Bowler. Louis Creekmur played ten seasons for the Lions and was famous for suffering at least 13 broken noses and 16 concussions. Beginning at the age of 58, he began to show increasing cognitive and behavioral difficulties including memory loss, problems with attention and organization, and outbursts of anger and aggression. He died from complications of dementia at the age of 82. The brain of Mr. Creekmur showed advanced CTE including marked shrinkage of medial temporal lobe structures that control memory, shrinkage of the frontal and temporal lobes, and marked dilation of the spinal fluid cavities that line the brain's interior. There was widespread and severe tau deposition as NFTs throughout the frontal and temporal lobes, amygdala, hippocampus, thalamus and brainstem in the unique pattern that is only found in CTE. In Mr. Creekmur's case, the abnormalities were extremely severe. There was absolutely no evidence of beta amyloid, Alzheimer's disease or any other neurodegenerative disorder, and the findings again indicated that if Mr. Creekmur had not sustained repetitive head trauma during the play of football, he would be alive and well and enjoying his family and grandchildren

today.



Lou Creekmur

Figure 3: Coronal sections of the brain of Louis Creekmur stained for phosphorylated tau protein show dense abnormalities throughout the brain. Bottom row: microscopic views of abnormal tau deposits. There was extensive nerve cell loss and advanced neurodegenerative changes throughout the brain.

Case 4. Dave Duerson, former defensive back Chicago Bears

Dave Duerson began playing football at age 8 and played a total of 24 total seasons as a safety in college and as a defensive back in the NFL. He experienced more than 10 concussions in his 11-year NFL career, several with loss of consciousness, although he was never admitted to hospital. After retiring from the NFL, he was very successful in the food supply industry (Duerson Foods), active in NFL Players Association and Benefits Board; he had a loving family with three sons and a daughter and was considered in generally good health. In 2007, he began

to experience business and financial difficulties that culminated in the loss of his business and the dissolution of his marriage. He was known to be smart, charming, kind and gentle but he became progressively more hot-tempered, physically and verbally abusive. He began to experience memory lapses; mood swings, piercing headaches on the left side of his head, difficulty spelling simple words, and blurred eyesight. On February 17, 2011, Duerson killed himself inside his Florida apartment at age 50. He left a note that carried a request: "Please, see that my brain is given to the NFL's brain bank " (The VA CSTE brain bank). The request was accompanied by an unusual method of suicide; he shot himself in the heart. At autopsy, his brain showed extensive changes of moderately advanced CTE, without evidence of any other disorder including Alzheimer's disease (Figure 4).

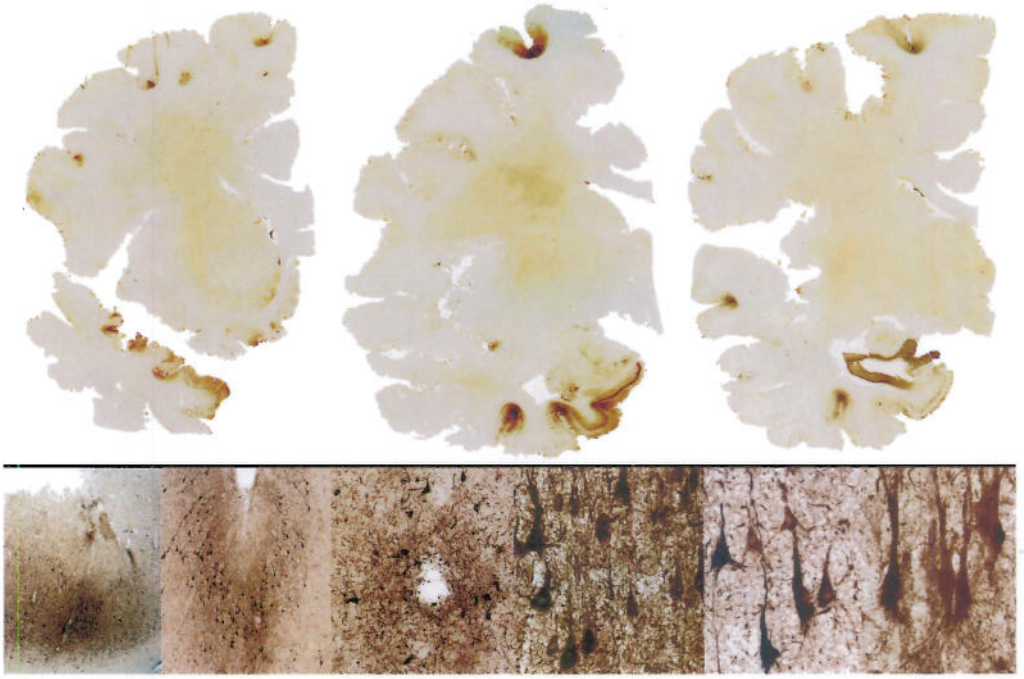


Figure 4: Coronal sections of the brain of Dave Duerson stained for phosphorylated tau protein show dense abnormalities throughout the brain. Bottom row: microscopic views of abnormal tau deposits showing extensive abnormalities of tau in nerve cells and support cells.

Case 5. Owen Thomas, defensive end University of Pennsylvania

Owen Thomas was a University of Pennsylvania defensive end who loved football and had played football since age 9. He was considered to be the life of the team and was unanimously voted team captain. There was no history of documented or undocumented concussion, depression or psychiatric difficulties, and no evidence of substance abuse. One day in the spring of 2010, he called his parents and told them he was stressed by school and having trouble with several of his subjects, two days later he hanged himself in his off campus apartment. Neuropathological examination of Owen's brain showed the unmistakable changes of early CTE with focal collections of NFTs in multiple areas of his frontal cortex and evidence of spread of the NFTs to adjacent cortical regions (Figure 6). Comparison of the brain of Owen Thomas to the brain of Dave Duerson shows remarkable similar pathology and suggests that if Owen Thomas had lived another 30 years, his CTE would have progressed to the moderately severe stage demonstrated by Dave Duerson.

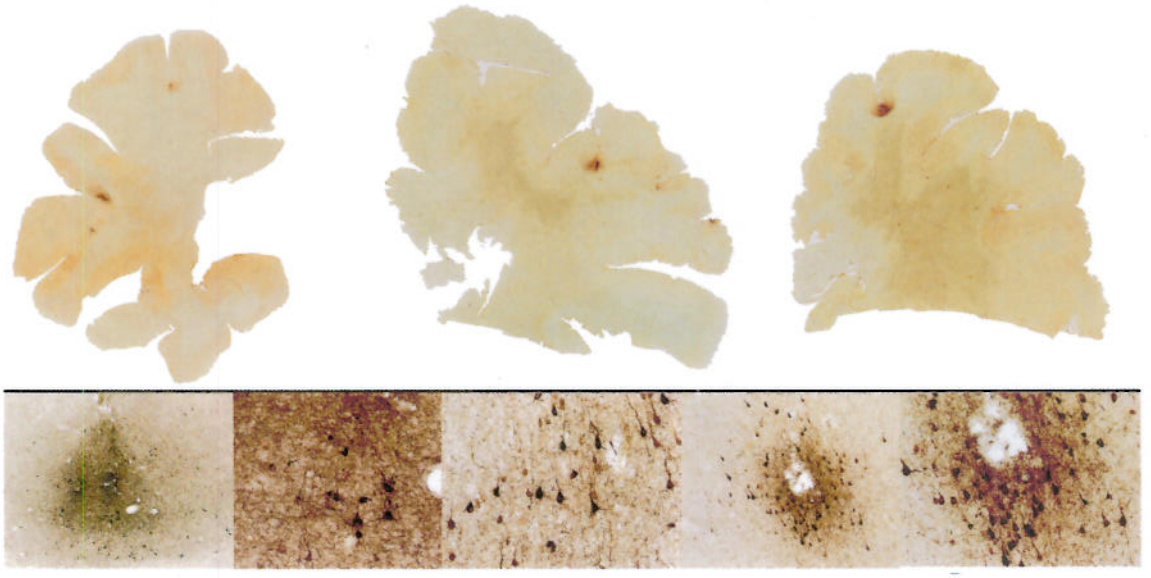
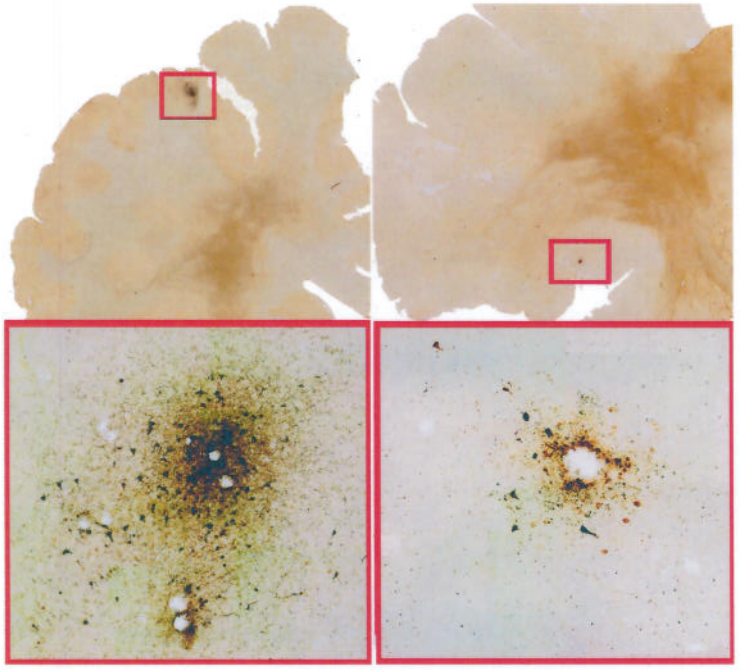


Figure 5. Coronal sections of the brain of Owen Thomas stained for phosphorylated tau protein

show dense abnormalities throughout the brain. Bottom row: microscopic views of abnormal tau deposits. There was extensive nerve cell loss and advanced neurodegenerative changes throughout the brain.

Case 6. 18-year-old high school football player

I also have had the opportunity to examine the brain of a high school football player who died at the age of 18. He had played football and other sports for 4 years and suffered several concussions. The brain of an 18 year old should be pristine; there should be no abnormalities whatsoever. But in the brain of this young man, there were several areas of damage in the frontal lobe that you could see even looking at the slides with your naked eye (Figure 6, top row). In those areas, there were hundreds of degenerating nerve cells containing tau NFTs and disordered nerve cell processes indicative of early CTE.



18 year old

Figure 6. Brain sections from an 18 year old high school football and rugby player showing areas of damage in the frontal lobe (top row, red boxes), and microscopic views of views of phosphorylated tau containing NFTs in nerve cells and their processes in lower row.

Case 7. 17-year-old high school football player, death from Second Impact Syndrome (SIS)

A 17-year-old high school suffered a concussion 3 weeks before the day of his death and was cleared to return to play 2 days earlier. During the game, the running back and linebacker intercepted a pass and hit the ground. Nothing seemed exceptional about the tackle; it was considered a routine play. Yet as he walked to the bench, he complained of a severe headache and then collapsed to the ground unconscious. He died the following day. Neuropathological examination showed a thin subdural hemorrhage entirely consistent with Second-Impact Syndrome (SIS) and very early changes of CTE. He is the youngest player ever known to have changes of CTE on neuropathological examination.

SUMMARY

I have now examined the brains of 58 individuals with neuropathologically verified CTE - including 40 professional and amateur football players, 5 hockey players and 15 military veterans. I have found changes of early CTE in several college and high school football players, including early changes in players as young as 17 and 18 years. We know that CTE is a tauopathy and TDP-43 proteinopathy associated with repeated mTBI that most commonly occurs early in life, usually an individual's teens and early twenties. We know that once CTE is triggered, the neurodegeneration progresses slowly over decades to involve widespread degeneration of many brain structures. We know that the symptoms of CTE are often insidious and begin in mid-life with prominent early personality and behavioral changes, including irritability, short fuse, depression, suicidal ideations, impulsivity, and memory loss. We know there is a slow deterioration that may progress to include dementia, parkinsonism, gait and

speech disorders. However, there remain many things that we do not understand about CTE. An autopsy case series will never establish incidence and prevalence of this disorder, even though we now clearly understand that CTE exists - and that it is surprisingly common. What factors determine who will develop CTE - how many concussions or how many subconcussive injuries, how close together the injuries are, how severe, and at what age – all of these are aspects of this disease that are unknown at this time. Most importantly, we do not know how to diagnose this disease in living individuals, how to stop its progression or how to reverse its course at the present time. But we can make important changes to prevent this disease from developing in young athletes, and those changes include understanding what a concussion is, recognition of concussion when it occurs, and proper medical management of concussion after it happens. We can also teach our young athletes to play smart and to keep their head out of the game as much as possible. Rule changes to protect athletes from dangerous styles of play, rule enforcement and player and coach education will go a long way towards reducing the frequency of concussion. With these changes in the way sports are played, continued education, increased scientific research into the mechanisms of CTE pathogenesis, and the development of diagnostic tools and therapeutic strategies to interrupt disease progression, we can make an enormous improvements to protect the mental health of millions of young athletes and military service members for many years to come.

References

1. McKee AC, Cantu RC, Nowinski CJ, Hedley-Whyte ET, Gavett BE, Budson AE, Santini VE, Lee H-Y, Kubilus CA, Stern RA. Chronic Traumatic Encephalopathy in Athletes: Progressive Tauopathy following Repetitive Head Injury. *J Neuropath Exp Neurol*, 2009 68(7): 709-735.

2. McKee A, Gavett B, Stern R, Nowinski C, Cantu R, Kowall N, Perl D, Hedley-Whyte E, Price B, Sullivan C, Morin P, Lee H-S, Kubilus C, Daneshvar D, Wulff M, Budson A. TDP-43 Proteinopathy and Motor Neuron Disease in Chronic Traumatic Encephalopathy, Journal Neuropathol Exp Neurol, 2010, 69: 918-929.

Authors' reply: McKee AC, Budson AE, Gavett BE, Stern RA, Daneshvar D, Nowinski CJ, Cantu RC, Kowall NW, Perl DP, Hedley-Whyte ET. J Neuropathol Exp Neurol. 2011 Jan; 70(1): 98-100.

3. Gavett, B, Stern R, Cantu R, Nowinski C, McKee A. Mild traumatic brain injury: A risk factor for neurodegeneration, Alzheimer's Research and Therapy, 2010, Jun 25; 2(3): 18.

4. Gavett B, Stern R. McKee A. Chronic Traumatic Encephalopathy: A Potential Late Effect of Sport-Related Concussive and Subconcussive Head Trauma. Clinics in Sports Medicine, 2011 Jan; 30(1): 179-88, xi.

5. Daneshvar D, Nowinski C, McKee A, Stern R, Cantu R. Helmets and Mouth guards: The Role of Personal Equipment in Preventing Sports Related Concussions. Clinics in Sports Medicine, 2011 Jan; 30(1): 145-63, x.

6. Cantu RC, Gean AD. Second-Impact Syndrome and a Small Subdural Hematoma: An Uncommon Catastrophic Result of Repetitive Head Injury with a Characteristic Imaging Appearance. J Neurotrauma 2010 27:1557–1564.

7. Chaiwat O, Sharma D, Udomphorn Y, Armstead WM, Vavilala MS. Cerebral hemodynamic predictors of poor 6-month Glasgow Outcome Score in severe pediatric traumatic brain injury. J Neurotrauma 2009 26(5): 657-63.