

A Review of Chronic Traumatic Encephalopathy and its Growing Impact in Football Players

Elizabeth Akinmerese¹ and Sonya Loughran^{1#}

¹Colleyville Heritage High School

#Advisor

ABSTRACT

Chronic Traumatic Encephalopathy (CTE) is a neurodegenerative, progressive disease diagnosed after repetitive head impacts (RHI). While the diagnosis of CTE can only be confirmed by a neuropathologic examination of brain tissue during an autopsy, it has a burgeoning impact on the football society. This paper details the fatalistic influence of CTE on football players, emphasizing the game's most prominent organization, The National Football League (NFL). This article aims to present the effects of CTE, including but not limited to motor symptoms, cognitive impairment, and neuropsychiatric features, while statistically analyzing its influence in many former professional players.

Introduction

CTE is a neurodegenerative progressive disease encountered in people who undergo repetitive head impacts (RHI) and repeated episodes of concussions, such as NFL players, military services, and other close-contact activities. However, not all people who experience RHI go on to develop CTE; some studies have shown no increased incidence of CTE in people exposed to RHI. Although many clinical signs and symptoms are associated with CTE, it cannot officially be diagnosed in living people; the diagnosis of CTE is ensured only by a neuropathologic examination of brain tissue after death through an autopsy. The development of CTE has been linked to second-impact syndrome (where a second head injury occurs before the previous head injury fully resolves). Researchers do not know how often CTE is proposed in the population and its specific causes, therefore no cure exists ("Chronic Traumatic Encephalopathy - Symptoms and Causes," 2016).

Development and Manifestation of CTE Within the Brain

The Neuropathology of CTE

To understand how CTE presents itself in the brain, we must understand what a healthy brain is. Neurons act as the basic building block of the brain and are responsible for sending and receiving neurotransmitters (chemicals that carry information throughout the brain). Composed of three significant parts: the cell body, the axon, and the axon terminal, neurons are accustomed to specific characteristics that allow them to maneuver the chemicals across the brain by sending signals down its axons and off to the nearby cells (Lovinger, D. M. 2008). The lengthy and spindly shape of the axon may help the neuron reach far-away cells; however, the structure weakens its strength, making it prone to injuries during an intense head impact. Damage to the axon results in complications that hinder its ability to send signals, interfering with the body completing regular functions ("The Science of C.T.E.," 2018).

Microtubules are rigid hollow rods within the brain and serve as a neuron transportation system. The dynamic structures are under various forms of assembly and disassembly in the brain while moving essential materials throughout the cell body, axon, and axon terminal. Due to microtubules' small diameter (approximately 25nm), they are more

prone and vulnerable to damage during a concussion (Cooper, n.d.). Under normal conditions, the proteins that support the microtubules' structure, microtubule-associated protein tau (MAPT), aid in microtubule stabilization. MAPT is phosphorylated more than expected in abnormal situations; when these new hyperphosphorylated tau (p-tau) proteins disconnect from microtubules in the axon, they aggregate into neurofibrillary tangles (NFTs), astrocytic tangles (A_{ts}) and neurites around small blood vessels (McKee, A. C, 2015). The dissociation of p-tau is a vicious cycle, and it has been proven that when tau aggregates, it takes on other tau aggregates and evades numerous areas of the brain (Katsunoto, A, 2019).

Correlation between effected areas of the brain and neurological symptoms

In 2013, in a case series of 68 male donors, Dr. Ann McKee, a neuropathologist and the director of the CTE Center at Boston University (BU CTE Center), proposed a pathological staging system on a scale from 1(mild) - 4(severe) that characterized the density and regional depositions of the p-tau and analyzed the effects of CTE. The distribution of p-tau follows age-dependent continuations; older age is more associated with the later and more severe stages of CTE (Alosco, 2020).

1. This is the earliest stage of CTE, where patients will experience memory loss as a cause of isolated p-tau lesions in 1 or 2 foci and speckled neurites gathered around microscale blood vessels, frequently found in the frontal lobe and cortex (Alosco, 2020). Headaches occur, explosive behaviors and depressive moods develop, and executive function (organizational skills, judgment, multitasking, and planning) declines.
2. The foci of p-tau lesions expand and spread to multiple cortical regions, such as superficial NFTs residing within the adjacent cortex, causing short-term memory difficulties to become more prominent (Alosco, 2020). Alterations in mood are common, and some people begin to note a tendency towards suicidal thoughts and substance abuse, along with experiencing impaired judgments and loss of speech articulation.
3. In stage 3, perivascular clusters of NFTs, A_{ts}, and neurites are found at the sulcal depths. Distributed NFTs, characterized as lesions, have taken over the medial temporal lobe structures (Alosco, 2020), causing sudden violent actions, paranoia, and erosion of memory. Cognitive dysfunction, mood changes, issues with visuospatial function, and apathy intensify.
4. CTE has spread to numerous brain parts, and its effects are detrimental because the perivascular p-tau lesion and NFTs consume the cerebral cortex. These p-tau lesions and NFTs also extended toward the diencephalon, brainstem, and spinal cord (Alosco, 2020). Cognitive dysfunction becomes severe; memory loss may progress to dementia, challenges with gait (movement may become uncoordinated and slow), and visuospatial function worsen. Aggression and explosive outbursts may also intensify in some individuals.

According to Madeline Uretsky, the Research Program Manager at the Boston University CTE Center, specific symptoms become known based on one's age when the initial hit occurs. For example, some people live into their 80s and develop dementia, while others die earlier and have don't have the pathology that relates to progressive cognitive symptoms that indicate dementia.

Overall Symptoms of CTE

Chronic Traumatic Encephalopathy is linked to numerous symptoms, including suicidal thinking, memory failure, and assertive demeanors. Multiple individuals diagnosed with CTE have been proven to have cognitive, behavioral, temper,

and motor shifts. CTE is a progressive illness implying that the symptoms can arrive long after the initial collisions to the head.

Motor Symptoms

Identified, in many cases, is motor instability. The sufferer has trouble swallowing, declining speech articulation, and coordination impairment. Motor symptoms also include Parkinsonism, a group of conditions like those exhibited in Parkinson's disease (bradykinesia, rigidity, and tremors). The most common problems involved gait and balance (51%), dysarthria (23.5%), and signs of Parkinsonism (up to 28%) (Katz, 2021).

Cognitive Impairment

The patient experiences episodic memory concentrating, comprehending new things, and lessened speech and visuospatial function (reported in more than 60% of the cases) (Katz, 2021). Difficulty thinking and memory loss cause the patient to lose their executive function, which includes organizational skills, judgment, multitasking and planning.

Neuropsychiatric Symptoms

In over 40% of the autopsy identified CTE, the deceased person developed behavioral dysregulation problems and impulsive actions, including explosive outbursts, rage, and apathy. Patients undergo depression, start misusing substances, and experience emotional instability leading to suicidal thoughts that increases the risk of self-inflicted death (Katz, 2021).

Supportive Features Used in Determining Provisional Levels of Certainty for CTE Pathology

According to the National Institute of Neurological Disorders (NIND) paper on Traumatic Encephalopathy Syndrome (TES), the following three supportive features are used in determining the provisional levels of certainty for CTE. These symptoms are frequently present in individuals with underlying CTE pathology.

Delayed Onset – A established period of stable functioning after the repetitive head impacts end where the progression of symptoms has not been established.

Motor Signs - Parkinsonism which includes bradykinesia, rigidity, and rest tremor. Other motor signs include dysarthria (weakening speech muscles), ataxia (loss of muscle control withing the arms and legs), and imbalance.

Psychiatric Features - These supportive psychiatric should represent an apparent change from baseline and be persistent or progressive. Psychiatric features include anxiety, apathy (loss of interest and motivational drive), depression, and paranoia. These features include excessive worry, interest loss, sadness, and delusional suspicions.

Impacts on the NFL and Sub-Organizations – Known Statistics

Former Study Conducted by The Boston University CTE Center (2017)

In an article published in 2017 by The Journal of the American Medical Association (JAMA), Dr. Ann McKee, a neuropathologist at Boston University, dissected the brains of 202 deceased football players (median age at death: 66

years). CTE was neuropathologically diagnosed in 177 players (87%) with an average football participation of 15.1 years. Of the 202, 111 played professionally in the NFL, and 110 (99%) were found to have CTE. Using data from the JAMA article titled, “Clinicopathological Evaluation of Chronic Traumatic Encephalopathy in Players of American Football,” the following graphs layout the quantitative data received from the BU CTE Center study on 202 brains.

Table 1: 2017 C.T.E Diagnosis Statistics

Football Organization (Highest Level of Play)	Number of Players Participated Players	Number of C.T.E Diagnosis	Percentage
Pre-High School	2	0	0%
High School	14	3	21%
College	53	48	91%
Semi-Professional	14	9	64%
Canadian Football League	8	7	88%
National Football League (N.F.L)	111	110	99%

NFL "speed players" such as quarterbacks, fullbacks, and halfbacks are at a greater risk of getting tackled at elevated accelerations continuously and have a higher potential to develop CTE compared to others.

Table 2: 2017 Neuropathological Severity in No. Brains

Football Organization (Highest Level of Play)	Mild Severity	Severe Severity
High-School	3	0
College	21	27
Semi-Professional	4	5
Canadian Football League	1	6
National Football League	15	95

- I. Mild CTE (neuropathological stages 1 & 2) is characterized by sparse frequent lesions at the sulcal depths of the cerebral cortex.
- II. Severe CTE (neuropathological stages 3 & 4) is characterized by multiple lesions in the cerebral cortex.

The 110 CTE diagnosed NFL brains within the analysis executed by Dr. Ann McKee had significant findings in their documentation regarding symptoms; nearly all were found to enclose substantial neurological and psychological developments. 86% of the patients' next-of-kin reported that their symptoms became detrimental over time.

Table 3: 2017 Reported Clinical Features in No. Brains

Reported Clinical Features	Mild Severity	Severe Severity	Total
Cognitive	23	80	103
Memory	19	76	95
Executive Function	19	67	86
Dementia	9	71	80
Impulsivity	23	65	88
Suicidality	15	21	36
Motor	13	63	76
Parkinson's Disease	1	5	6

- I. There were 111 participants with standardized informant reports: 27 mild cases and 84 severe cases.
- II. For mild cases sample sizes ranged from 25-27
- III. For severe cases sample sizes ranged from 78-84

An analysis of only former NFL players in this study with CTE pathology was frequently severe, suggesting that these brain-related injuries result from prior participation in football and that at a heightened level of play, the risk towards CTE increases substantially. Additional research has exhibited that age at first exposure may be related to deficient cognitive performance. For comparison, in 2018, the BU CTE Center conducted an analysis containing 164 brains of men and women (not targeting football players). Donated to the Framingham Heart Study, only 1 of the 164 (0.6) had CTE. The CTE diagnosed case was found to be a former college football player, supporting the assertion that receiving repeated collisions to the head during physical activity highly increases the evolution of CTE (Mann, 2023).

Recent Study Conducted by The Boston University CTE Center (2023)

On February 6th, 2023, The BU CTE Center reported that the 110 diagnosed former NFL players with CTE had advanced to 345 deceased persons out of 376 studied brains (91.7%). This data should not be interpreted as 91.7% of all (current and former) NFL players have CTE, as the study uses samples from brain banks where selection biases occur (“Researchers Find CTE in 345 of 376 Former NFL Players Studied,” 2023). The rapid prevalence of CTE is unknown because CTE can only be confirmed after death. Of the 345 former diagnosed players, all have been reported to have manifestations of memory loss, confusion, aggression, depression, and suicidality, whereas more severe cases have progressed to dementia.

Information regarding an in-depth breakdown of neuropathological severity and statistical analysis of reported clinical features have not been released to the public, however, Dr. Ann McKee claims, “While the most tragic outcomes in individuals with CTE grab headlines, we want to remind people at risk for the CTE that those experiences are in the minority.” (“Researchers Find CTE in 345 of 376 Former NFL Players Studied,” 2023).

Current attempts made by physicians and the NFL committee

The league has frequently faced neurological damage within its players and has taken several measures to diminish the risk of trauma-inflicting head impacts. According to an official statement by the NFL., they have made "47 rule changes since 2002 to protect players, improve practice methods, better educate players and personnel on concussions and strengthen the league's medical protocols... Working with the N.F.L. Players Association, the league enforces a concussion protocol for players that has been instrumental in immediately identifying and diagnosing concussions and other head-related injuries."

In 2015 the N.F.L. was required to compensate former players who encountered neurological damage, such as C.T.E., with an authorized \$1 billion settlement plan (Abdalazem, 2022).

In 2016 the N.F.L. Commissioner, Roger Goodell, appointed the \$100 million 'Play Smart. Play Safe' action to propel advancement in stemming, diagnosing, and treating brain-related injuries, alongside supporting medical research and engineering advancements. Supported by four pillars: protecting players, advanced technology, medical research and sharing progress, the 'Play Smart. Play Safe' action has significantly improved the health and wellbeing of professional athletes ("NFL Announces Play Smart. Play Safe., n.d).

Football is hazardous, and the league may never be free of brain damage, but the league will continue to refine the game to make it safer for not only professional athletes, but for those who are just starting the game. However, refined protocols and equipment help alleviate the risk of concussions and overall brain deterioration (Abdalazem, 2022).

Episodes of Actual Experience

Among those diagnosed within the past year are two former players who represented the same teams paired in the Super Bowl LVII championship, former Philadelphia Eagles quarterback Rick Arrington (1970-73) and former Kansas City Chiefs defensive tail Ed Lothamer, who was present at Super Bowl IV ("Researchers Find CTE in 345 of 376 Former NFL Players Studied," 2023). Rick Arrington's daughter, sportscaster Jill Arrington, declared that though he had no account of concussions, her dad suffered from CTE for over 35 years. "His life was cut short but the sport he loved," she lamented (Mann, 2023).

Aaron Hernandez– Aaron Hernandez, a former New England Patriots tight end and convicted murderer was found dead on April 19, 2017, hanging from a bedsheet in his prison cell. A postmortem brain scan revealed that Hernandez had been suffering from the worst case of CTE in a young person the BU CTE Center had ever seen. Hernandez, who was only 27 years old at the time of his suicide was riddled with stage 3 CTE to a degree that "we've never seen...in our 468 brains, except for individuals very much older," stated Dr. Ann McKee (Bracken, 2017.) The scan, showed evidence of brain atrophy, damage to the frontal lobe, and large portions of black spots created by tau protein. During his lifetime Hernandez showed signs of depressions, migraine, and memory loss.

Junior Seau– At the time of Junior Seau's suicide on May 12th, 2012, the former NFL linebacker was found to have been suffering from CTE after over 20 seasons in the league. Seau's brain was donated to the National Institute of Health, where his brain scan showed he had build-ups of the tau proteins. His ex-wife reported that during his lifetime, Seau received a lot of head-to-head collisions, leading to depression and presenting signs of dementia (Fainaru-Wada, 2013).

Limitations and Conclusions

This review has some limitations. Data used in the "Former Study by the Boston University CTE Center (2017)" only retains a quantitative analysis of documented cases of CTE (as of 2017), leaving out potential cases that had yet to be discovered, including the additional diagnoses present in the 2023 case study. A complete comparison between the 2017 and 2023 studies is minimal, as there is insufficient data. Additional information, such as a breakdown of neuro-pathological severity and reported clinical features, regarding the newly discovered CTE case as of 2023 has yet to be released by the BU CTE Center.

In finalization, Chronic Traumatic Encephalopathy is a neurodegenerative disease caused by multiple blows to the head leading to the disconnect of hyperphosphorylated tau (p-tau) proteins from microtubules, which then aggregate into neurofibrillary tangles and astrocytic tangles invading numerous areas of the brain. CTEs' enduring presence in the NFL and subsequent organizations has significantly affected former players, calling for action toward safety precautions. A cure for CTE has yet to be found; however, the NFL has taken several steps in the right direction by enforcing safer equipment and newer protection procedures to protect current and future players.

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