Potential Long-Term Consequences of Concussive and Subconcussive Injury

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KEYWORDS

• Neuropathology • Trauma • Traumatic brain injury
• Chronic traumatic encephalopathy • Tau • Concussion • Subconcussion

KEY POINTS

- Individuals with a history of repetitive head impacts are at risk for developing chronic traumatic encephalopathy (CTE).
- CTE is a unique neurodegenerative disorder characterized by perivascular deposits of hyperphosphorylated tau at the depths of the cerebral sulci.
- The number of years of exposure to contact sports, not the number of concussions, is significantly associated with more severe tau abnormality in CTE, suggesting that repetitive head trauma, including subconcussive injury, is the primary driver of disease.
- Recent studies in neurodegenerative disease brain bank cohorts suggest that changes of CTE are relatively common.

Over the last decade, there has been considerable interest in the potential long-term effects of concussive and subconcussive injury that occur in association with the play of contact sports. Case reports and case series have described athletes who developed explosivity, loss of control, aggressive and violent behaviors, impaired attention,

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depression, executive dysfunction, and memory disturbances associated with chronic traumatic encephalopathy (CTE). There have been debates about how commonly CTE occurs, whether CTE is a distinct neurodegeneration, and if the repetitive head impacts that occur during the play of sports are causal to CTE development. The disease symptoms lack specificity, and the absence of longitudinal, prospective clinical studies with neuropathologic analysis limits understanding of the full clinical spectrum. However, current data indicate that the neuropathology of CTE is unique and can be readily distinguished from other neurodegenerative diseases; that exposure to repetitive head impacts, not the number of concussions, is the primary driver of CTE abnormality; and that CTE is more common than currently recognized.

The variety of clinical symptoms associated with boxing was first described by Harrison Martland[1] in 1928, who found abnormalities in "nearly one half of the fighters who stayed in the game long enough."[1] The general public referred to the condition as "punch drunk," "goofy," and "slug-nutty,"[2,3] and later the terms "dementia pugilistica"[4] and "chronic traumatic encephalopathy" or "CTE" were introduced.[5] Over the intervening decades since the recognition of CTE, clinical and neuropathologic evidence has emerged indicating that CTE occurs in association with American football, boxing, wrestling, ice hockey, baseball, and soccer. CTE has also been associated with other forms of mild repetitive head injury, such as physical abuse, epileptic seizures, head banging, and activities related to military service.[6–12]

CLINICAL SIGNS AND SYMPTOMS OF CHRONIC TRAUMATIC ENCEPHALOPATHY

The clinical symptoms of CTE typically develop insidiously, years to decades after exposure to repetitive brain trauma, and progress slowly over years to decades.[13–15] Occasionally, persistent symptoms develop while an individual is still active in a sport that may be difficult to distinguish from prolonged post-concussive syndrome.[16] In the authors' series of 119 neuropathologically confirmed CTE cases, the mean age at symptom onset was 44.3 years (standard error of the mean [SEM] = 1.5, range 16–83 years), 14.5 years after retirement from the sport (SEM = 1.6, n = 104). However, 22% of individuals later diagnosed with CTE were symptomatic at the time of retirement. The clinical course is often protracted (mean duration = 15.0 years, SEM = 1.2, n = 125).[14,17,18] It is unclear what factors mitigate the wide age range of clinical onset, and many are the focus of current research investigation. Genetics may play a role in an individual's relative susceptibility or resistance to the adverse effects of repetitive neurotrauma and factors such as cognitive reserve, including educational attainment and environmental enrichment, and age at first exposure may influence the clinical expression of the disease.

The clinical presentation of CTE characteristically begins in one or more of 4 distinct domains: mood, behavior, cognitive, and motor. Early behavioral symptoms include explosivity, verbal and physical violence, loss of control, impulsivity, paranoia, and rage behaviors.[15,19] Cognitively, the most prominent deficits are memory, executive functioning, and impaired attention. Approximately 45% of subjects with CTE develop dementia; of subjects older than the age of 60 years, 66% develop dementia. Complaints of chronic headaches occur in 30%[15]; motor symptoms, including dysarthria, dysphagia, coordination problems, and parkinsonism (tremor, decreased facial expression, rigidity, and gait instability), may also develop.[20]

Stern and colleagues[15] distinguished 2 courses of clinical presentation. The first type presents with mood and behavioral symptoms early in life (mean age = 35 years) and progresses in severity to include cognitive symptoms later in the disease course. The second course presents with cognitive symptoms later in