Chronic Traumatic Encephalopathy: A Potential Late Effect of Sport-Related Concussive and Subconcussive Head Trauma

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KEYWORDS

- Encephalopathy, Post-traumatic
- Neurodegenerative disorders • Concussion • Athletic injuries
- Dementia • Motor neuron disease

It has been understood for decades that certain sporting activities may increase an athlete's risk of developing a neurodegenerative disease later in life. Not surprisingly, this association was originally noted in boxers, athletes who receive numerous blows to the head during training and competition. In 1928, Harrison Martland, a New Jersey pathologist and medical examiner, first described the clinical spectrum of abnormalities found in "nearly one half of the fighters who have stayed in the game long enough."[1]

This work was supported by NIA P30AG13846, Supplement 0572063345-5, National Operating Committee on Standards for Athletic Equipment, and by the Department of Veterans Affairs. This work was also supported by an unrestricted gift from the National Football League. The funding sources were not involved in the preparation, review, or approval of this article.

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Clin Sports Med 30 (2011) 179–188
doi:10.1016/j.csm.2010.09.007 **sportsmed.theclinics.com**
0278-5919/11/$ – see front matter. Published by Elsevier Inc.

Boxers exhibiting cognitive, behavioral, or motor abnormalities were well known to lay persons, sportswriters, and others within the boxing community and were referred to by various terms, such as "punch drunk," "goofy," and "slug-nutty"[2,3]; later, the more formal term *dementia pugilistica* was introduced to lend medical validity to the condition.[4] By the 1970s, a sufficient number of boxers with dementia pugilistica had been studied pathologically to support the conclusion that this form of neurodegeneration was similar to, but distinguishable from, other causes of neurodegenerative disease.[5] As evidence of the clinical and neuropathologic consequences of repeated mild head trauma grew, it became clear that this pattern of neurodegeneration was not restricted to boxers, and the term chronic traumatic encephalopathy (CTE), originally coined by Miller[6] became most widely used.

Over the last several 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, and head banging.[7–13] Although the incidence and prevalence of CTE is currently unclear, it probably varies by sport, position, duration of exposure, and age at the time of initial or subsequent head trauma, and with additional variables, such as genetic predisposition. To date, there have been no randomized neuropathologic studies of CTE in deceased athletes, and as such, there is a selection bias in the cases that have come to autopsy. If one considers the prevalence in deceased professional American football players who died between February 2008 and June 2010, there were 321 known player deaths[14] and the brains of 12 of the 321 underwent postmortem neuropathologic examination at Boston University Center for the Study of Traumatic Encephalopathy (BU CSTE). All 12 examined neuropathologically showed evidence of CTE, suggesting an estimated lifetime prevalence of at least 3.7%. If one assumes that all deceased players who did not come to autopsy did not have CTE and that the amount of head trauma in professional football has remained fairly constant over the past 5 decades, a prevalence of 3.7% would result. Although this represents a conservative estimate, it suggests a significant public-health risk for persons who suffer repetitive mild traumatic brain injury (TBI).

CLINICAL SIGNS AND SYMPTOMS OF CTE

Whereas concussion and postconcussion syndrome represent temporary states of neuronal and axonal derangement, CTE is a neurodegenerative disease that occurs years or decades after recovery from the acute or postacute effects of head trauma. The exact relationship between concussion and CTE is not entirely clear, although repetitive axonal perturbation may initiate a series of metabolic, ionic, membrane, and cytoskeletal disturbances, which trigger the pathologic cascade that leads to CTE in susceptible individuals.[15,16] The onset of CTE is often in midlife, usually after athletes have retired from their sport. In some individuals, the early manifestations of CTE affect behavior; in particular, individuals with neuropathologically documented CTE have been described by family and friends as being more irritable, angry, or apathetic or as having a shorter fuse. Increased suicidality seems to be a particularly salient symptom of CTE.[17] In other cases, cognitive difficulties may be the first signs to emerge, with poor episodic memory and executive functioning being two of the most common cognitive dysfunctions reported. Later in the disease, movement (eg, parkinsonism), speech, and ocular abnormalities may emerge in the context of declining cognition and worsening comportment. A minority of cases with neuropathologically documented CTE developed dementia before death; the relative infrequency of