

A survey of former NFL players raises questions about diagnoses of degenerative brain disease

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A postmortem exam of the brain remains the gold standard for diagnosing chronic traumatic encephalopathy, or CTE, the

neurodegenerative brain disease believed to arise from repeated hits to the head.

Yet a small but by no means trivial number of former professional football players say they have received a [diagnosis](#) of CTE, according to a new study from Harvard Medical School and the Harvard T.H. Chan School of Public Health published April 13 in *Annals of Neurology*.

The research—based on a survey of nearly 4,000 former NFL players, ages 24 to 89—was conducted as part of the ongoing Football Players Health Study at Harvard University, a research initiative that encompasses a constellation of studies designed to evaluate various aspects of players' health across the lifespan.

Even though the results are based on player self-reports rather than on documented clinical diagnoses, the researchers say their findings are alarming for a number of reasons.

First, CTE is a post-mortem diagnosis and cannot be diagnosed definitively in living individuals. Second, an erroneous, or clinically unverifiable, diagnosis of CTE could obscure the role of other treatable conditions common among former football players that could cause a cluster of cognitive and [behavioral symptoms](#) mimicking CTE. Third, delivering a verdict of an untreatable disease could render patients hopeless, discouraging them from pursuing healthy behaviors and focusing on modifiable risk factors and conditions that may give rise to symptoms attributed to CTE.

Researchers emphasize that any cognitive and behavioral symptoms should be investigated thoroughly, and CTE concerns should never be dismissed.

"Former football players are rightfully worried about brain health and

CTE concerns should not be overlooked, yet in the absence of validated clinical criteria and diagnostic methods for CTE, the fact that former players report being told they have the disease is highly concerning," said study lead author Rachel Grashow, a researcher at the Harvard T.H. Chan School of Public Health. "A diagnosis of CTE could downplay the effects of other conditions and discourage the pursuit of alternative explanations, while creating a sense of despair among those who believe they might have an untreatable brain condition."

Nearly 3 percent of the players in the current study (108 out of 3,913) reported they had received a diagnosis of CTE from a physician or another clinician. Those older than 60 were more likely to report a CTE diagnosis than younger players (3.7 percent, compared with 2.3 percent).

Symptoms of cognitive impairment—difficulty concentrating, forgetfulness, mood changes—were notably more common among former players who reported CTE diagnoses, regardless of age. Those who reported a CTE diagnosis were also more likely to report sleep apnea, heart disease, hypertension, stroke, depression, [high cholesterol](#), obesity, use of prescription pain medication and low testosterone.

All of these are relatively common in former football players and can cause certain cognitive symptoms, which could be fueling clinical suspicion for CTE among some physicians, the researchers said. Given that safe and effective interventions exist for many of these conditions, it is critical that these patients are evaluated and treated before cognitive problems are prematurely or wrongly attributed to CTE.

Former players who self-identified as Black had higher percentages of CTE diagnoses, the study found. Researchers said the higher prevalence of conditions such as [high blood pressure](#), diabetes and cardiovascular disease among Black men may explain the higher rate of CTE diagnoses in this group.

The current study was not designed to determine why or how the CTE diagnoses were made. The researchers, however, say a number of factors could be at play.

For example, some clinicians may suspect the presence of CTE because past studies have identified a link between neuropsychiatric symptoms in the decade preceding an athlete's death and subsequent postmortem CTE diagnosis. Also, clinicians may be seeing certain behavioral and cognitive changes as markers of brain degeneration, propelling them to consider a CTE diagnosis, while downplaying or not fully exploring alternative explanations for the symptoms, such as sleep apnea, heart disease or depression. Clinicians may also be more likely to consider—and suggest—CTE to players who spent their careers in more high impact positions, the researchers said.

Lack of clarity about symptoms and possible causes might leave patients prone to over-interpretation and set the stage for misunderstanding, the researchers said.

"Given the high visibility and intense media coverage of CTE, former football players may be highly sensitive to any hints or suggestions of CTE and assume a connection between their symptoms and this rather high-profile, but not necessarily accurate or appropriate, diagnosis," Grashow said. "Either way, it is incumbent upon the physicians who care for former athletes to ensure that such clarity is achieved."

None of this is to say that some former players may not, in fact, have CTE.

"CTE is real, and it probably plays a role in the cognitive or behavioral symptoms experienced by some former players, yet many of these symptoms could also arise from a number of other, more treatable, conditions," said study senior author Ross Zafonte, head of the

Department of Physical Medicine and Rehabilitation at Spaulding Rehabilitation Hospital and Harvard Medical School.

Zafonte cautioned that a grim diagnosis like CTE could magnify symptoms, a psychological phenomenon known as the nocebo effect. It could also discourage people from engaging in healthy behaviors and pursuing critical treatments for other conditions responsible for the symptoms, added Zafonte, who is also principal investigator of the Football Players Health Study.

First described in the 1920s as boxers' dementia or "punch-drunk syndrome," CTE gained public attention over the last 20 years after a series of reports identified the hallmarks of the disease—abnormal protein clumps in certain parts of the brain—in postmortem exams of former football players, many of whom had shown cognitive, emotional and behavioral symptoms for more than a decade prior to their postmortem exams. CTE develops predominantly in people who sustain repeated blows to the head, including athletes in contact sports such as boxing, football, hockey and rugby, in military personnel who sustain head trauma and in victims of domestic violence.

More information: Rachel Grashow et al, Pre-mortem Chronic Traumatic Encephalopathy Diagnoses in Professional Football, *Annals of Neurology* (2020). [DOI: 10.1002/ana.25747](https://doi.org/10.1002/ana.25747)

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