Over the past decade, the sports medicine community has dealt with a very worrisome knowledge gap: that between those who suffer concussions playing football and the postmortem findings of chronic traumatic encephalopathy (CTE) in former National Football League (NFL) players. At one end of the spectrum, we know that football players sustain regular head trauma, and as a medical community, we have become more aware of the acute consequences and clinical course of these events. On the other end, the postmortem CTE findings in some deceased football players understandably generate great concern among football players, their families, the sports medicine community, and American society in general. Our knowledge gap centers on the lives and well-being of those between the 2 ends of the spectrum: living, retired NFL players. Some theorists have already connected the dots, concluding that football concussions lead to CTE. Consequently, a thorough examination of living, former NFL players has the potential to answer several troublesome questions about the natural history of concussion.

Is there a detectable course of mental deterioration after football? Can this course be correlated with objective findings on physical examination or imaging studies? Some of this critical information on the health and well-being of retired, former players has been supplied in previous studies. However, these surveys must be scrutinized because of their lack of clinical correlation and known methodological shortcomings. In short, in those studies, players were surveyed but not examined. Those studies do not correlate the trends that they detect with objective physical examination or imaging study findings.

A study by Hart et al attempted to fill the knowledge gap with an evaluation of 34 retired, living NFL players using neuroimaging to detail cognitive dysfunction and depression. They used neurologic and neuropsychologic assessment along with neuroimaging in a subset (26 players) in comparison with 26 healthy controls. They found cognitive deficits and depression more common in aging former NFL players than healthy controls, generating obvious cause for concern.

The most recent study by Casson et al deserves special attention because of the extent of the examinations performed. Forty-five former NFL players were studied as a convenience sample in an age range from 30 to 60 years. They had played in the NFL for an average of $6.8 \pm 3.2$ years and sustained an average of $9.0 \pm 6.9$ concussions in their football careers, which included an average of $12.2$ years before the NFL. Thirty-four of the 45 had sustained 3 or more concussions at the NFL level. So even though this was a convenience sample, this group had played a lot of football and had sustained a significant amount of head trauma in an era when concussion treatment was far from the current standard of care.

This study by Casson et al was designed to be a very thorough evaluation, including magnetic resonance imaging, susceptibility weighted imaging, diffusion tensor imaging, neuropsychologic and neurologic physical examinations, interviews, and apolipoprotein E (APOE4) genotyping. It was modeled after a previous study of boxers by the same author but with much more technical sophistication. The boxer study found signs of brain damage in 16 of 18 active and former pugilists. Without a doubt, this current study by Casson et al is the most extensive evaluation of former NFL players focusing on the effects of head trauma in football.

The results of the study by Casson et al are quite telling. They appear to document the course of repeated head trauma while painting a more optimistic picture than recent studies and press reports. The majority of players had normal clinical mental status and neurologic examinations. Most important, none of these players demonstrated signs of dementia, dysarthria, Parkinsonism, or cerebellar dysfunction. Evidence of significant head trauma was clear, however, with 4 football players showing signs of microbleeds in the brain parenchyma. Unfortunately, 3 showed brain atrophy with a large cavum septum pellucidum, similar to that seen in boxers. However, 87% showed no magnetic resonance imaging evidence of chronic brain trauma.

Depression has been implicated as the cause of the demise and tragic deaths of several former NFL players. Twenty percent of this study group did show signs of moderate to severe depression. Whether the depression was caused by previous football exposure, their loss of limelight once their NFL careers ended, or some other factor is unknown. Nevertheless, this is cause for concern and demonstrates the need for mental status monitoring by those responsible for the medical care of former players.
This study also examined blood samples for the APOE4 allele. Carriers of this allele are thought to be at increased risk of developing Alzheimer disease with head trauma.\textsuperscript{6,7} Thirty-eight percent of the retired players carried this marker, which is higher than the 23\% to 26\% expected in the general population, raising the concern of a genetic susceptibility to head trauma. If there is a genetic susceptibility component to these debilitating conditions and CTE, it may explain why some players appear to be immune despite their long-term careers in football. Their genetic makeup may protect them and prevent mental deterioration.

The use of neuropsychologic testing has become common after concussion and appears to be most helpful in those with slow recovery and chronic problems. Eleven players (24\%) showed isolated impairments in this study, which could be related to brain trauma. Interestingly, the statistics suggest that these impairments were more likely related to body mass index and ethanol use, demonstrating the difficulty in isolating the effects of common comorbidities.

Overall, there was a statistical association between abnormalities on the central nervous system examination and the total number of concussions experienced at all levels of football, emphasizing the importance of the physical examination’s potential for former players and those still active in the sport. Careful monitoring of these abnormalities may help complete the picture of the natural history of concussion and its relationship with CTE.

Most important, this study appears to refute the current belief, held by many, that the cumulative effect of concussion in NFL players results in chronic brain injury. While 13\% showed objective evidence of brain trauma, 87\% did not, despite the use of very sensitive techniques for detecting injured brain tissue.

To put this study in perspective, its generalizability has to be questioned. Is it representative of the thousands of retired NFL players? One of the study’s limitations is the fact that only 45 players were included. Despite this shortcoming, it does appear to be a reasonable representation of those who played NFL football in terms of their pre-NFL experience, years in the league, and number of sustained concussions. What will happen to this group in years to come remains of high interest, since the average age in this group was 46 years; there is still time for more problems to surface clinically.

Thankfully, most players in this group did not show evidence of organic brain damage. Time and more careful research will tell if this holds true for this group of players and others who played on the gridiron.

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Editor-in-Chief

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