A Focus on Football Injury

Both scientific studies and recent news events about the long-term results of head injuries in professional contact sports have focused public and professional attention on imaging approaches to understanding the complex causes of neurodegeneration after trauma. A study published in the February issue of the *American Journal of Geriatric Psychiatry* (2013;21:138–144) explored the utility of PET in in vivo detection of tau protein deposits in the brains of retired professional athletes who had mood and cognitive symptoms suggestive of traumatic brain injury (TBI). The study, authored by Small and researchers from the David Geffen School of Medicine at the University of California, Los Angeles, and others, was widely covered by the popular media and followed a series of well-publicized studies focusing on TBI and chronic traumatic encephalopathy (CTE) in athletes.

Small and colleagues' study group included 5 retired players from the National Football League (NFL) (ages, 45–73 years; a linebacker, guard, center, defensive lineman, and quarterback), each of whom had a history of behavioral, mood, and/or cognitive symptoms suggesting alteration as a result of repeated trauma to the head. Each player underwent neuropsychiatric evaluation as well as ^{18}F-FDDNP PET imaging. PET results from these individuals were compared with those from 5 cognitively normal men of comparable age, education, and body mass index. Specific brain areas for image comparison included the subcortical and cortical regions. The researchers found that PET signals were higher (uptake was greater) in players than in controls in all subcortical regions and the amygdala—those areas in which tau deposits are evident after trauma.

"Early detection of tau proteins may help us to understand what is happening sooner in the brains of these injured athletes," Small told the *New York Times.* "Our findings may also guide us in developing strategies and interventions to protect those with early symptoms, rather than try to repair damage once it becomes extensive." The authors noted the limitation of their small sample size and concluded that future research is needed to confirm their findings that ^{18}F-FDDNP PET offers a unique means for premorbid identification of neurodegeneration in contact sports athletes.

In an article e-published on December 2 ahead of print in *Brain*, McKee and a consortium of researchers from the Veterans Affairs Boston Healthcare System (MA) reported on a post mortem evaluation of brains from 85 individuals with histories of repetitive mild TBI and found pathologic evidence of CTE in 68 brains (64 of which came from professional athletes). A control group of 18 brains came from age- and sex-matched individuals without histories of repetitive TBI. The researchers demonstrated that in brains with evidence of CTE, tau pathology varied from isolated focal perivascular epicenters of neurofibrillary tangles in the frontal neocortex to severe and dense pathology affecting widespread brain regions, including the medial temporal lobe. These variations allowed progressive staging of CTE. The researchers found multifocal axonal varicosities and axonal loss in deep cortex and subcortical white matter at all stages of CTE. The stage of CTE correlated directly with increased length of time spent playing football. In 43 brains, CTE was the sole diagnosis (63%). Eight were also diagnosed with motor neuron disease (12%), 7 with Alzheimer disease (11%), 11 with Lewy body disease (16%), and 4 with frontotemporal lobar degeneration (6%). The authors concluded that "The frequent association of CTE with other neurodegenerative disorders suggests that repetitive brain trauma and hyperphosphorylated tau protein deposition promote the accumulation of other abnormally aggregated proteins including TAR DNA-binding protein 43, amyloid-beta protein and alpha-synuclein."

The wide media coverage of both the Small et al. and the McKee et al. studies focused public attention on the implications for current and retired players of contact sports, with extensive attention to recent suicides among retired NFL players with cognitive and mood impairments. On January 29, the NFL Players Association (NFLPA) announced an award of $100 million to Harvard University to create a 10-year research initiative to be called the Harvard Integrated Program to Protect and Improve the Health of NFLPA Members. The program will be aimed at the discovery and identification of new approaches to diagnosing, treating, and preventing injuries and illnesses in both active and retired players. "Our goal is to transform the health of these athletes," said Lee Nadler, MD, Harvard Medical School dean for clinical and translational research, who will direct the program. "In order to extend the life expectancy and quality of life of NFLPA members, we must understand the entire athlete, all the associated health risks, and all of their interactions. We refer to this comprehensive approach as the 'Integrated NFL Player'." Experts from diverse fields, including imaging, epidemiology, genetics, metabolomics, lipidomics, cell biology, neurobiology, regenerative medicine, neuroscience, and computational biology, will participate in the program. Researchers plan to initially partner with NFL players to identify a group of at least 1,000 retired athletes from across the country. From this group, researchers will identify 100 healthy and 100 unhealthy players and, through a series of studies, create what the researchers describe as a "biological profile of illness." These and other projects are designed to yield near-term results and will be followed by other innovative studies, identified through competitive academic challenges issued to researchers both within and outside the Harvard system.