Neuroimaging technique identifies concussion-related brain disease in living brain

September 16 2014

An experimental positron emission tomography (PET) tracer is effective in diagnosing concussion-related brain disease while a person is still alive, according to a case study conducted at the Icahn School of Medicine at Mount Sinai, and at Molecular Neuroimaging (MNI) LLC in New Haven, and published September 16 in the journal *Translational Psychiatry*.

Specifically, the study results suggest that an experimental radiolabeled compound called [18 F]-T807, which is designed to latch onto a protein called tau that accumulates in the brain with repetitive blows to the head, can be registered on a PET scanner to effectively diagnose chronic traumatic encephalopathy (CTE). The study results also argue the process can differentiate it from other forms of dementia while the sufferer is still alive. Until now, CTE diagnosis has only been possible by evaluating post-mortem brain tissue.

"Our data suggest that PET imaging using the [18F]-T807 tau tracer is an effective method of diagnosing or ruling out chronic traumatic encephalopathy in a living brain," says Samuel Gandy, MD, Director of the Center for Cognitive Health and NFL Neurological Care at the Icahn School of Medicine at Mount Sinai. "Estimates of the prevalence of CTE have varied wildly, with the most recent figure coming from the National Football League who predicts that one in three NFL players will suffer significant brain damage. We can now begin to test this while

the players are still alive. Moreover, we are now equipped to tell prospective athletes of all ages some real data on the risks that accompany sports involving repeated traumatic brain injuries."

Signs of CTE were originally spotted in boxers and retired National Football League (NFL) players. Before their deaths, many of these athletes struggled with symptoms like memory loss, depression, and violent outbursts, and in some cases they became suicidal. The NFL is currently helping to launch large-scale studies of the condition. More recently, the brains of ice hockey players and battlefield veterans exposed to repeated bomb blasts have revealed evidence of CTE.

In recent years, scientists have developed radiotracers like [18F]-T807 that attach to protein aggregates and emit high-energy particles called positrons that are registered on a PET scanner. The [18F]-T807 tau tracer selectively binds only to tangles of tau in the brain and not to amyloid proteins associated with Alzheimer's disease, making it superior to other proposed tau tracers to date in terms of CTE detection, according to the study authors.

The Mount Sinai case study included the evaluations of two living patients, a retired NFL football player with a history of multiple concussions and a patient with a single, severe traumatic brain injury (TBI). Both patients presented with cognitive decline and suspected AD. Both were evaluated by a combination of molecular imaging techniques to pinpoint specific brain disease and damage

Brain injury, whether as a result of repeated head trauma or a single, traumatic brain event, may jumpstart a process whereby tau protein, which functions in a healthy brain to help stabilize a nerve cell's protein skeleton, breaks off the skeleton and begins to build up inside nerve cells. The theory is that tangles of tau protein accumulate and cause nerve cell damage in the CTE brain.

While various dementias like CTE and AD share many symptoms, the nature and distribution of brain degeneration in chronic traumatic encephalopathy is distinctive from AD. CTE is characterized by prominent formation inside nerve cells of structures called tangles, a process called a tauopathy. The dementia of CTE occurs in midlife after a latency period of years or decades after exposure to repetitive head trauma.

In this study, led by Dr. Gandy, both patients underwent neurologic and neuropsychological assessments by a team of TBI and AD experts. Following this comprehensive evaluation, the experts disagreed as to whether AD was present in this retired NFL player.

Both patients underwent PET imaging with florbetapir, another chemical that is FDA-approved to detect the brain amyloid plaques of Alzheimer's disease during life. In the case of the retired NFL player, who suspected he had AD and presented to the team at Mount Sinai in hope to participate in a clinical study for AD, the florbetapir PET scan was negative for cerebral amyloidosis, thereby excluding AD and the possibility of his engaging in a treatment protocol for his suspected, incorrect AD diagnosis. He also underwent [18F]-T807 PET imaging that revealed signs of aggregated tau in some temporal areas of his brain.

The current study is the first where one technology was able to show both the abnormal accumulation of tau protein in a person that experienced several concussions in the distant past, while at the same time demonstrating that the patient did not have the protein signature seen with Alzheimer's disease.

"Although we are just now understanding the clinical impact of PET, our use of tauopathy PET imaging to evaluate the progressive alterations in brain proteins for CTE patients already offers us a powerful new tool for evaluation," says Ken Marek, MD, President and Senior Scientist at

Molecular Neuroimaging (MNI) LLC in New Haven, where the [18F]-T807 imaging was performed. "In particular, we can directly measure the accumulation of tau protein we believe associated with the devastating symptoms experienced by patients and their families and evaluate the disease during life in ways that were previously only available to the pathologist's microscope."

A tauopathy imaging program at Mount Sinai Hospital is expected to commence in early October, 2014.

Researchers from the University of Virginia also contributed to the study.

Provided by The Mount Sinai Hospital