

# Experimental imaging agent reveals concussion-linked brain disease in living brain

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An experimental positron emission tomography (PET) tracer can effectively diagnose concussion-related brain degeneration while a person is still alive, according to a proof-of-concept study conducted at the Icahn School of Medicine at Mount Sinai and published September 27 in the journal *Translational Psychiatry*.

Mount Sinai researchers used an experimental imaging agent called [18 F]-T807 (or Avid 1451) with PET to examine the brain of a living, 39-year-old retired National Football League (NFL) player who had experienced 22 concussions and exhibited clinical symptoms consistent with chronic traumatic encephalopathy (CTE), a neurodegenerative brain disease that has been associated with repetitive blows to the head in athletes and soldiers. T807 is designed to latch onto a protein called tau that accumulates in the brain as a result of repetitive traumatic brain injury. When the new imaging agent (or ligand) lights up a PET scan of the brain of a patient showing buildup of tau in a characteristic pattern, the scan result is interpreted as being consistent with CTE. Until now, evidence for CTE pathology has only been possible by examining brain tissue after death.

CTE has a distinctive pattern of tau deposition that was described in 2015 by an expert panel commissioned by the National Institute of Neurological Disorders and Stroke (NINDS). That panel laid out diagnostic criteria for CTE based on samples of postmortem brain tissue.

The surface of the brain is highly wrinkled. The tau accumulation in CTE appears to trace the highly folded surface of the brain and is especially concentrated at the deepest points in the wrinkles and folds. The NINDS panel used the word "pathognomonic" to describe the CTE tau pathology pattern. This is a technical term that indicates that whenever you see this pattern of tau pathology, the diagnosis can be nothing other than CTE. There can be no confusion with other tau diseases.

"Our study participant's scan is the first to reveal during life a pattern of tau imaging that outlines the wrinkles and folds of the living brain, just like the 'pathognomonic pattern' described by the NINDS panel as diagnostic of a brain with CTE," says Sam Gandy, MD, Director of the Center for Cognitive Health and NFL Neurological Care Program at the Icahn School of Medicine at Mount Sinai and last author of the study. "When fully validated, this new ligand has the potential to be used as a diagnostic biomarker and represents an exciting development in the detection and tracking of CTE."

A link between [brain injury](#) and long-term health has gained greater attention in recent years, helped along by evidence of neurofibrillary tangles of tau protein, or tauopathy, that has been clinically confirmed in the postmortem brain tissue of former athletes and soldiers with histories of multiple head traumas. In addition to symptoms such as irritability and extreme mood swings, CTE is associated with the symptoms of various other neurodegenerative diseases, including Alzheimer's, Parkinson's and Lou Gehrig's diseases.

"This research is in its infancy," says Dara L. Dickstein, PhD, Assistant Professor of Neuroscience, and Geriatrics and Palliative Medicine at the Icahn School of Medicine at Mount Sinai and first author of the study. "Whether or not the pathology can be reversed or halted is something we have yet to determine and these new tauopathy PET scans may be able to

help in this endeavor."

Under the leadership of Drs. Gandy and Dickstein, and with primary funding support from the Alzheimer's Drug Discovery Foundation (ADDF), Mount Sinai is one of the few medical centers researching the use of the new ligand in living patients who are believed to have CTE. The Mount Sinai team is currently studying 24 patients and plans to establish a clinical trial early next year that will employ the new ligand to identify CTE patients who might respond to an anti-tauopathy medicine that is currently being studied at other medical centers for the treatment of Alzheimer's disease and other neurodegenerative disorders.

"These findings demonstrate that we may now have the first biomarker for the detection of CTE through tau imaging," says Howard Fillit, MD, ADDF's Founding Executive Director and Chief Science Officer. "This may prove significant as an early diagnostic tool for those who suffer repeated traumatic brain injuries. It may also help us better understand the similarities in disease processes between CTE, Alzheimer's and other neurodegenerative diseases, and determine whether repeated head injuries may lead to the onset of Alzheimer's."

Provided by Mount Sinai Health System

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