

## Health Headlines

For Immediate Release  
February 28, 2020



**Sam Gandy, MD, PhD**



**Gregory Elder, MD**

### **Brain Scan-Blood Test Panel Promises Improved Diagnosis of Brain Trauma Following Battlefield Blast Exposure**

*New brain scans and blood tests move researchers towards more sensitive diagnosis of battlefield brain trauma and evaluation of new drugs*

BRONX, NY – An array of tests that combines functional assessment with blood tests and brain scans promises more sensitive and objective estimation of brain degeneration in human veterans exposed to battlefield improvised explosive device (IED) blasts, according to research led by doctors at the Icahn School of Medicine at Mount Sinai and the James J. Peters VA Medical Center. The study was published in *Molecular Psychiatry* on Tuesday, February 25, and featured on the journal's cover.

Traumatic brain injury (TBI) is associated with acute brain destruction at the time of the injury and is also a risk factor for developing neurodegenerative diseases later in life. It is estimated that 10 to 20 percent of veterans returning from the conflicts in Iraq and Afghanistan sustained mild TBI resulting from IED and other

blast exposures. The true prevalence may be even higher, given that many blast-related injuries go undocumented. Symptoms of mild TBI frequently resolve in days to months following injury, but in a subset of patients, symptoms persist and evolve into a chronic syndrome. Veterans who had sustained TBIs may suffer subtle, yet important, endocrine and neuropsychiatric dysfunction. Given the fact that suicide rates have jumped substantially among young military veterans in recent years, it is imperative to develop earlier, more objective and sensitive methods to detect brain damage.

Using advanced methods of clinical neuropsychological and neurocognitive assessment, brain imaging, and blood biomarker measurement in veterans of the Middle East conflicts, together with modeling of mild repeated blast injury in laboratory rats, the researchers found changes in the brains and blood of those subjected to blasts. Specifically, they performed neuroimaging and blood analysis of human veterans who were exposed to IED blasts on the battlefield and on rats exposed to repetitive, low-level blasts in a shock tube. All veterans reported histories of between 1 and 50 blast exposures, and all had chronic behavioral and cognitive complaints.

Two chemical changes that occur during neurodegeneration involve clumping of a brain protein called tau and leakage of another protein called neurofilament protein-light chain (Nf-L) from the brain into the blood. The research team used positron emission topography (PET) and the [18F]AV1451 (flortaucipir) tau ligand, a molecule which produces a signal by binding to a site on the tau protein that “lights up” on a PET image, and found that 5 of the 10 veterans exhibited excessive retention of [18F]AV1451 at the white/gray matter junction in frontal, parietal, and temporal brain regions, a typical localization where tau protein clumps tend to accumulate after TBI. In healthy brains, tau is essential for normal cell functioning, helping stabilize the internal skeleton of nerve cells in the brain, but when tau proteins build up and clump together, it causes the internal skeleton to collapse and form twisted tau tangles that promote brain cell damage.

As an additional biomarker, they measured blood levels of Nf-L, since elevated levels of Nf-L have been reported in human patients suffering from a variety of brain injuries, including mild TBI and neurodegenerative diseases. They observed elevated levels of Nf-L in the plasma of veterans displaying excess [18F]AV1451 retention. The human component of the study was led by Sam Gandy, MD, PhD, Professor of Neurology, and Psychiatry, and Director of the Center for Cognitive Health and NFL Neurological Care at the Icahn School of Medicine at Mount Sinai, Attending Neurologist at the James J. Peters VA Medical Center, and co-senior author of the paper.

In parallel, the research team examined a rat model being studied by Gregory Elder, MD, Professor of Neurology, and Psychiatry, at the Icahn School of Medicine at Mount Sinai, Chief of Neurology at the James J. Peters VA Medical Center, and co-senior author of the paper. The rat model was designed to mimic a level of blast exposure that would be comparable to a mild TBI or a subclinical blast exposure in

humans. Rats exposed to this blast protocol exhibit a range of anxiety and behavioral traits resembling post-traumatic stress disorder. Dr. Elder and colleagues found that rats exposed to repetitive, low-level blasts accumulated abnormal tau in nerve cells as well as around blood vessels in cells called astrocytes. Astrocytes play important roles in supporting nerve cells and during inflammatory events.

“We are fortunate to have access to both living humans and living rodent models so that we can conduct side-by-side comparisons of the clinical and microscopic changes that are common to both species related to traumatic brain injury,” said Dr. Gandy. “As a result of these parallel studies in veterans and in the Elder brain injury model, we are well on our way to the first clinical trials wherein first-in-class drugs will be evaluated for their safety and for their potential clinical benefit in relieving the anxiety, depression, memory disorders, and anger management issues that are associated with traumatic brain injuries.”

Previous research conducted by Dr. Gandy and his colleagues identified some of the first PET images of protein aggregates in the brains of living athletes and veterans with histories of TBI, consisting primarily of either the tau protein or, alternatively, a protein called amyloid beta. Amyloid beta is the main component of brain plaques associated with Alzheimer’s disease, while tau is the main constituent of neurofibrillary tangles, which are hallmarks of the neurodegenerative diseases frontotemporal dementia and chronic traumatic encephalopathy (CTE). For now, CTE can only definitively be diagnosed postmortem, but one goal of this research conducted by Drs. Gandy and Elder is to find methods for effective diagnosis while patients are still alive.

“There are many young, otherwise healthy veterans who have suffered blast-related TBIs, some of them years in the past, who either aren’t getting better or, in some cases, are getting worse,” says Dr. Elder. “We don’t know why or how to identify those at greatest risk. The work in this study is a step towards answering those questions.”

For this project, the human studies were conducted by Dara Dickstein, PhD, Adjunct Assistant Professor of Neuroscience at the Icahn School of Medicine at Mount Sinai.

Following blast exposure, the rats were studied by Rita De Gasperi, PhD, Instructor in Psychiatry at the Icahn School of Medicine at Mount Sinai and the James J. Peters VA Medical Center.

“This research supports the Alzheimer’s Drug Discovery Foundation mission by identifying biomarkers — like brain neuroimaging — that can lead to earlier diagnosis of Alzheimer’s and related dementias, including CTE,” said Howard Fillit, MD, Founding Executive Director and Chief Science Officer of ADDF, one of the study’s financial supporters. “CTE research is relatively new, but it is advancing rapidly. Studies such as this one will advance our understanding of CTE, Alzheimer’s and other neurodegenerative diseases, improve the rigor and efficiency of

clinical trials, and may ultimately provide screening tools to identify patients for the trials and as a measurement to assess drug effect.”

The study was primarily supported by the Alzheimer’s Drug Discovery Foundation and the Department of Veterans Affairs.

### **About the James J. Peters VA Medical Center**

The Bronx (James J. Peters) VAMC is a tertiary care medical center classified as a Clinical Referral Level 1b facility that provides a broad range of inpatient and outpatient health care services. The Medical Center health serves an estimated 171,000 Veterans throughout the North Metropolitan New York area, including Bronx, Westchester and Rockland Counties, as well as parts of Northern New Jersey, Queens and New York Counties. The facility serves nearly 26,000 unique Veterans providing approximately 350,000 outpatient visits annually. The facility supports three Community Based Outpatient Clinics, and a \$29.4 million Research program, including a MIRECC, GRECC and a Spinal Cord RR&D Center of Excellence. The Medical Center hosts one of seven VA renal transplant programs and serves as the regional referral center for Spinal Cord Injury, MS, ALS, TBI and Polytrauma, Amputee Care, Bariatric, Microvascular and Robotic Surgery. The medical center has 250 operating hospital beds plus 80 operating Community Living Center (CLC) beds with a budget of over \$330 million. The JJP VAMC enjoys a formal and longstanding affiliation with three major academic institutions in New York City. Our affiliations with The Icahn School of Medicine at Mount Sinai School and the Mount Sinai Health System, the Hospital of Special Surgery, and Columbia University Vagelos College of Physicians and Surgeons and New York Presbyterian Hospital, provide academic support for medical student and resident training programs.

For more information related to this story or the James J. Peters VA Medical Center, please contact Jim Connell, Public Affairs Officer, at [jim.connell@va.gov](mailto:jim.connell@va.gov)

#####