<http://www.ninds.nih.gov/news_and_events/news_articles/CTE_found_in_veterans.htm>

National Institute of Neurological Disorders and Stroke

**First cases of degenerative brain disease CTE found in veterans with blast injuries**

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Some veterans who experience blast-related head injuries on the battlefield can develop the same kind of long-term brain damage seen in athletes who have had multiple head injuries on the playing field.

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| U.S. Army soldier in AfghanistanA U.S. Army soldier in Afghanistan's Paktya province in May 2012. Photo by Spc. Eric-James Estrada, U.S. Army. Original photo at http://www.defense.gov. | This is one conclusion from a study led by Lee Goldstein, M.D., Ph.D., and Ann McKee, M.D., both of whom are faculty at Boston University (BU) School of Medicine.  The study expands the potential public health impact of chronic traumatic encephalopathy (CTE), which is the name for degenerative changes in the brain that are sometimes seen in people with a history of multiple concussions.  Until now, almost all of the data on CTE had come from case studies of athletes who spent many years, often a lifetime, in contact sports such as boxing, football and hockey.The new data “add to a sense of urgency to develop therapies,” said Dr. McKee, who directs the Neuropathology Service for the Veterans Affairs New England Healthcare System. |

CTE can only be diagnosed after death based on hallmark signs of damage in the brain.  Drs. McKee and Goldstein examined the brains of four deceased male veterans who had experienced blast injuries or other head injuries.  These cases were compared to four male athletes with a known history of head trauma and four men without such history.  The soldiers and athletes, but not the control cases, had the pathological markers for CTE.  The study was published in*Science Translational Medicine*[**\***](http://www.ninds.nih.gov/news_and_events/news_articles/CTE_found_in_veterans.htm#STM) and was supported in part by the National Institute of Neurological Disorders and Stroke (NINDS).

Research on CTE is still in an early stage; even the name is relatively new.  In the 1920s, researchers coined the name*dementia pugilistica* to describe a syndrome of dementia and other neurological symptoms seen in some boxers, years after their retirement from the sport.  The term CTE emerged in the 1960s when researchers realized that other kinds of repetitive head trauma can lead to a similar syndrome.

Many of the early symptoms of CTE are similar to those seen in an acute brain injury; they include problems with thinking and concentration, memory loss, headaches, irritability and depression.  However, CTE appears years or even decades after a head injury seems to have resolved.  As the disease progresses, it can lead to dementia, violent outbursts, and Parkinson's-like symptoms, such as poor balance and tremors.

Dr. McKee and her colleagues at the BU Center for Study of Traumatic Encephalopathy have confirmed more than 50 suspected cases of CTE among deceased individuals, mostly athletes, with a history of head injuries.

One hallmark of CTE is the presence of neurofibrillary tangles in the brain.  These are bundles of proteins that normally provide structural support inside brain cells.  In CTE, some of these structural proteins, particularly one called tau, become chemically altered in ways that cause them to clump and twist together.  There is recent evidence that once formed, this abnormal tau can spread throughout the brain.

Tangles containing tau are also seen in Alzheimer's disease, but in CTE, their distribution is different and they are concentrated near blood vessels.  Researchers theorize that this could indicate damage to the blood-brain barrier, a meshwork that lines cerebral arteries and veins and protects the brain from harmful substances in the bloodstream.

The four veterans in the current study had tau deposits and neurofibrillary tangles indistinguishable from those seen in athletes diagnosed with CTE.  All four of the soldiers had experienced multiple head injuries from various causes and three were diagnosed with post-traumatic stress disorder.  Three of the men had been exposed to improvised explosive device (IED) blasts during combat, and two of those three had suffered other head injuries earlier in life.  The fourth man was never exposed to a blast, but had sustained several concussions from bicycle accidents, sports and military combat.

The prevalence of CTE and its risk factors, aside from head trauma, are largely unknown.  Very few people with a history of head trauma are likely to develop CTE, but at the same time, it is conceivable that one or a few severe brain injuries could trigger the disease process, the researchers said.  The exact nature of the blow to the head, the person's age, sex, and genetics may all play a role.

Sorting out these factors through pathology studies would be impractical, Dr. McKee said.  These studies rely on brain tissue donated by the deceased individuals' families, who typically watched with concern as the affected person developed dementia and personality changes.  Studies on disease risk typically require large numbers of subjects, but few cases of CTE – and even fewer cases of head trauma without suspected CTE – are referred for evaluation.

Drs. McKee and Goldstein hope to address this challenge by studying a mouse model of CTE.  They were able to produce injury and abnormal tau in the brains of mice exposed to controlled blasts of compressed air, calibrated to generate about the same force as an IED several yards away.

"Now that we have a model, we're in a better position to develop tools to determine who is at risk," said Dr. Goldstein, who is a faculty member of the BU College of Engineering and a senior investigator at the NIH Alzheimer’s Disease Center, also at BU.

The researchers are using the mouse model to investigate how different mechanical forces on the head affect brain injuries and their long-term consequences.  They are also investigating steps in the disease process, with an eye toward new approaches for diagnosing and treating CTE.

The team discovered that exposure to even a single blast was sufficient to trigger brain pathology in the mice, including signs of damage to the blood-brain barrier.  An NINDS-funded project in Dr. Goldstein's lab will follow up on this finding and examine the mouse brains with a technique called metallomic imaging mass spectrometry (MIMS).  MIMS involves giving the mice injections of non-toxic gold nanoparticles that are too large to penetrate the intact barrier, and looking for the particles on brain scans to map leaky spots.  If MIMS confirms damage to the blood-brain barrier in the mice, future research could focus on therapies to repair the damage.

Dr. McKee is also involved in pilot studies following people at risk for CTE.  One such study is following 150 retired pro-football players, plus a control group of men, for five years.  That study will look for clinical signs of CTE, and will use magnetic resonance imaging (MRI) and other methods to look for potential CTE biomarkers.  A set of biomarkers – biological signs of disease that can be detected while the affected person is alive – would be useful for identifying the disease early and for developing treatments.  The study is funded in part by NINDS and is led by Robert Stern, Ph.D., who co-directs the BU Center for Study of Traumatic Encephalopathy with Dr. McKee.

*- By Daniel Stimson, Ph.D.*

\*Goldstein LE *et al*.  "Chronic traumatic encephalopathy in blast-exposed military veterans and a blast neurotrauma mouse model." *Science Translational Medicine*, May 2012, Vol. 4 (134), pp. 1-16.  DOI:[**10.1126/scitranslmed.3003716**](http://dx.doi.org/10.1126/scitranslmed.3003716).