

Researchers seek answers to complicated mental health condition

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Pathologist Dr. Ann McKee is part of the team behind VA's National PTSD Brain Bank. Credit: VA Boston Healthcare System

Understanding the complex nature of posttraumatic stress disorder, or PTSD, is one of the most pressing challenges for the U.S. Department of Veterans Affairs. An article in the October 2017 issue of *Current Psychiatry Reports* describes a resource aimed at providing answers: the

VA National PTSD Brain Bank.

The [brain-tissue](#) biorepository supports research on the causes, progression, and treatment of PTSD. The bank is responsible for [tissue](#) acquisition and preparation, diagnostic assessment, and storage. It's currently storing tissue from 168 brains, most of which are from people once diagnosed with PTSD. Many of the other donors had major depressive disorder. Other brains are from healthy controls.

More than 40 of the brains are those of veterans, about 75 percent of whom had PTSD. Most of the veterans who donated brains to the bank served in the Gulf War.

The bank is part of a consortium led by VA's National Center for PTSD at the White River Junction VA Medical Center in Vermont, one of the consortium's six participating sites. The other sites are the VA medical centers in Boston, the hub site; Miami; Durham, North Carolina; and West Haven, Connecticut, as well as the Uniformed Services University of the Health Sciences in Maryland. Tissue from the bank is sent to those sites as part of NPBB's intramural research program and is also disseminated to other investigators who conduct research in their own laboratories.

Dr. Matthew Friedman, the former executive director of the National Center for PTSD and now a senior advisor there, established the Brain Bank in 2014. He says it's the only one of its kind:

"We are the only PTSD [brain](#) bank in the world. None of the other 100-plus brain banks focus on PTSD."

The bank's main purpose, he says, is to advance understanding of the pathophysiology of PTSD - the study of how the disorder affects the brain. He says research on brain tissue from people with PTSD is critical

in developing new medications that treat the condition.

"There's a limit to what you can learn from [even] the most sophisticated brain imaging to understand what's different about people with PTSD, compared with people with depression or people with Parkinson's or healthy controls," Friedman says. "You want to learn what's different in terms of how they are processing information in key brain areas."

To do that, Friedman says, there's no substitute for analyzing brain tissue, for example, to gain a clearer understanding of how the RNA sequencing may differ. RNA, or ribonucleic acid, is a molecule key to the coding, decoding, regulation, and expression of genes. "You also have to look at the part of the gene that is actually activated," he says. "Different parts of different genes may be active or may be inactive."

Friedman was the lead author on the status report on the Brain Bank that appears in *Current Psychiatry Reports*. The report describes how the bank operates and highlights its accomplishments and its future challenges. One challenge calls for the facility to serve as a "major resource" for brain tissue research of people who had PTSD. To be certain that observed abnormalities are due to PTSD, rather than to some other cause, researchers must compare PTSD brains with tissue from healthy controls and with people who suffered from other psychiatric disorders, with or without PTSD, Friedman says.

Currently, six projects are underway that involve brain bank tissue. Researchers, for example, are looking at brain regions such as the prefrontal cortex, which helps regulate cognitive, emotional, and behavioral functioning, and the amygdala, which affects emotions, survival instincts, and memory. Improper functioning of those regions is linked to symptoms of the disorder.

Of the bank's two published studies to date, one focused on a gene that

has received limited attention in PTSD research: serum and glucocorticoid regulated kinase 1 (SGK1). Looking at postmortem brains from people with PTSD, the researchers found lower levels of the protein that is coded for by the gene. Preclinical tests with rats that lacked the gene and were exposed to stress supported the findings.

Yale University Professor Dr. Ronald Duman, a researcher at the National Center for PTSD, co-authored the 2015 study, which appeared in the journal *PLOS Biology*.

Friedman says the study found the rats that lacked SGK1 to be much more susceptible to fear conditioning. In this experimental technique, organisms learn to anticipate painful events such as an electric shock when exposed to a non-painful stimulus like a red light. The rats were also much less capable of fear extinction, or learning when the red light is no longer associated with electric shock. "This kind of experiment could not have been done or even conceptualized without looking at brain tissue from patients with PTSD," he says.

The PTSD bank is one of several VA facilities in Boston that stores brains. The others focus on the study of Alzheimer's disease; amyotrophic lateral sclerosis, also known as Lou Gehrig's Disease; Gulf War illness; traumatic brain injury (TBI); and chronic traumatic encephalopathy (CTE), a degenerative brain disease found in those with a history of repetitive brain trauma, such as football players, boxers, and service members exposed to blasts.

All of the Boston-based brain banks are programmatically linked and share staff, labs, and resources.

Friedman says the PTSD bank works most closely with the TBI-CTE brain bank. Such research is clinically relevant because so many veterans from recent wars suffer simultaneously from PTSD, TBI, and CTE, he

says. Future research in collaboration with the Alzheimer's bank will focus on PTSD in normal aging and in people who develop dementia, he notes.

"Probably one of the most respected neuropathologists in VA is Dr. Ann McKee," Friedman says. "Ann is the head of the TBI and CTE brain bank, and she's part of our group, as well. In other words, we're all part of one group. She might want some of our tissue from the PTSD bank. Likewise, we might want some of the tissue from the TBI bank, or if we're interested in aging some of the tissue from the Alzheimer's bank.

"People that work in the PTSD bank also work in some of these other banks," he adds. "The laboratories, equipment, and infrastructure overlap in many ways. It's a very, very efficient leveraging of resources."

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