Critical deposit *Dr. Ann McKee holds a research sample at a VA-hospital brain repository in Bedford, Mass.*

NATION

UNLOCKING THE SECRETS OF PTSD

New efforts to understand exactly how posttraumatic stress disorder affects the brain could reshape treatment for military veterans

BY MARK THOMPSON

DEEP INSIDE A BOSTON VA HOSPITAL, about two miles south of Fenway Park, four gray freezers are set at a constant temperature of –80°C. The chill protects the precious contents: samples donated to the nation's first ever brain bank for posttraumatic stress disorder (PTSD). There, scientists will dissect the brain tissues by shaving some into translucent slices resembling the pickled ginger served with sushi and turning others into chemical soups. Then they will become fodder for researchers trying to better understand what exactly goes wrong—at the cellular level—in the brains of people saddled with trauma.

The payoff could be immense. As many as 500,000 U.S. troops who served in the wars in Afghanistan and Iraq over the past 13 years have been diagnosed with PTSD. The toll can be enormous. Without adequate treatment, PTSD can ruin lives and destroy families.

The trouble for these veterans is that there is a dearth of adequate treatments, and what works for one person might not work for another. That's in part because when it comes to PTSD, there's still a lot that experts don't understand. Which is where the brain bank comes in. Scientists hope that investigating brains that once belonged to people with PTSD could yield important biological insights that might improve care for the hundreds of thousands of people who suffer from it.

"The burden of PTSD in service members who have been deployed in support of Operation Enduring Freedom in Afghanistan since 2001 and Operation Iraqi Freedom since 2003 is staggering," the National Academy of Sciences reported in an exhaustive 300-page study last June.

And while the U.S. spends $3 billion per year to treat the disorder in military veterans, just how that treatment is administered is uneven at best. Through its investigation, the report's authors discovered that some veterans were given

Photographs by Max Aguilera-Hellweg for TIME

treatments with scant evidence of their effectiveness. It's a chilling reminder that the government tends to be far better at deploying soldiers than at caring for them when they return.

In the case of PTSD, that's not entirely the government's fault. Though we have known for more than a century about the emotional wounds combat can inflict, we still don't fully understand the effects war has on the brain. There has long been debate over how much of PTSD is caused by physical changes in the brain and how much is tied to emotional responses to stress or trauma.

"We don't know the structural changes associated with PTSD because we haven't had this kind of brain bank before," says Dr. Ann McKee, a neuropathologist at Boston University who is overseeing the PTSD brain bank. "We've been diagnosing PTSD based on clinical symptoms, but we have not systematically characterized the pathology underlying this disorder."

McKee has studied the brain for decades. She did groundbreaking work on a degenerative brain disease caused by repeated head trauma that's commonly seen in football players and boxers. Now, with the PTSD brain bank, which received its first 10 brains on March 17 and is scheduled to begin operating this fall, McKee and her colleagues hope to learn how psychological trauma can change—and hurt—the brain too.

Those insights may eventually prove life-changing for soldiers with PTSD as well as countless civilians who are haunted by trauma caused by emotional and physical abuse, rape, violent attacks and serious accidents. Those who seek help are usually sent to group or individual therapy or both. Many will be prescribed potent medications, ranging from antipsychotics to antidepressants, in a search for a drug cocktail that may bring peace of mind. The uncertainty of what will work best for whom can make treating PTSD as much art as science. And since the consequences of not treating PTSD can be so dire—substance abuse, an increased risk of suicide—refining the science is critical. Which is why so much hope is resting on those freezers in Boston.

"There's kind of a desperation to get better treatment," says Alex Lemons, a 35-year-old former Marine from Salt Lake City who has wrestled with PTSD since the first of his three Iraq tours, in 2003. "This should have started decades ago."

Sample size *PTSD investigators will study thin slivers of brain tissue for evidence of physical changes*

As Old as War

PTSD CAN BE TRACED BACK TO ANTIQUITY. It was called "soldier's heart" during the American Civil War and morphed into "shell shock" in the First World War and "battle fatigue" during the Second. It became "operational exhaustion" in Korea and PTSD only after Vietnam, when the American Psychiatric Association added the term to its list of recognized mental disorders.

In a cruel twist, the increased skill of battlefield medics and surgeons has added to the ranks of soldiers with PTSD. With fewer troops dying from once fatal physical wounds, more have the bittersweet blessing of living with their combat memories. Among deployed troops, PTSD diagnoses grew by 400% from 2004 to 2012. The National Academy of Sciences report estimated that up to 20% of the 2.6 million U.S. men and women who served in Afghanistan and Iraq may have it. In 2011, 1 of every 4 veterans of the post-9/11 wars who sought help from the VA suffered from PTSD.

Some of that increase is likely due to changes that have broadened the diagnostic definition of PTSD. But most experts agree that the number of people who receive a PTSD diagnosis is far lower than the actual number of cases. That's in part because it can be a tricky condition to identify. Symptoms may appear soon after a traumatic event, or they may lurk until something—a new war, a flashback from an old one, something else altogether—rouses them from their torpor.

The severity of injuries also drives up PTSD rates: 8% among those with no wounds, 13% for those with penetrating wounds and 29% for those who experienced blunt-force trauma. Ground-pounding soldiers and Marines have PTSD at more than double the rate of sailors and airmen. And the condition is the third most common service-connected disability, after hearing loss and tinnitus.

While PTSD is not limited to the armed forces—victims of all manner of trauma experience it—only veterans suffer from PTSD because they did their government's bidding. Which is why some leaders in the field have long argued that it's the government's responsibility to invest in more meaningful research and treatment for people with PTSD.

For years, doctors have been pushing for a government-backed brain bank to study PTSD—and pointed to the important research breakthroughs from the more than 50 brain banks in the U.S., many privately funded, for maladies like Alzheimer's and depression. "We have favored getting a brain bank going for a long time, but nobody in government seemed interested," recalls Richard Weidman, the executive director of policy at the nonprofit Vietnam Veterans of America. "They don't want to pay for PTSD."

Matthew Friedman ran the Department of Veterans Affairs' National Center for PTSD in White River Junction, Vt., from 1989 to 2013. In 2004 he wrote that increasingly sophisticated functional-MRI imagery revealed a "neurocircuitry of fear and anxiety" inside live human brains. Figuring out why neural networks crank up so high in those with PTSD, he argued, requires methodical brain dissection and analysis. In other words, a brain bank.

Yet neither the Pentagon nor the VA pushed for its creation, and neither, when asked by TIME, could explain why. "The problem," Friedman says, "was getting secure funding."

That finally changed last year, when Vermont Senator Patrick Leahy, a senior Democrat on the Appropriations Committee, added $1.5 million to the federal budget to create what will become the VA's Leahy-Friedman National PTSD Brain Bank. "We spend a lot of time, money and effort getting men and women ready to go to war," Leahy says. "I've always felt that we ought to devote more attention as well to helping them when they come home."

Hunting for the Source

THE BRAIN HAS ALWAYS BEEN A CHALlenging puzzle for researchers. The electrical impulses and biochemical reactions of the brain, sealed inside the skull, run both body and mind. Their interplay, wrote Charles Sherrington, a Nobel Prize–winning early 20th century brain researcher, is "an enchanted loom where millions of flashing shuttles weave a dissolving pattern, always a meaningful pattern, although never an abiding one, a shifting harmony of subpatterns."

PTSD disrupts those harmonious interactions among the brain's 100 billion cells, generating symptoms ranging from hypervigilance to depression to sleeplessness. Its insidious and multiple manifestations (there are up to 636,120 symptom combinations, two psychologists calculated in 2013) make PTSD especially vexing to treat.

"PTSD evolves based on the cultural conditions of the people who suffer through it," says David Morris, a former Marine who chronicled his condition in the book *The Evil Hours: A Biography of Post-Traumatic Stress Disorder*. "The neuroscience for PTSD is less clear than it is for manic depression or Alzheimer's."

At the brain bank in Boston, McKee and her team will try to answer some of the biggest questions about PTSD. Why are some people more vulnerable to it and some more resilient? How much of the way we react to any traumatic event is the result of biological factors, and how much is environmental?

The researchers will initially rely on 50 brains from Baltimore's Lieber Institute for Brain Development, a nonprofit that has more than 500 brains stockpiled for research into schizophrenia. Eventually, the brain bank plans to set up a website where veterans will be able to volunteer their own brains for study after they die. The government will pay Lieber about $20,000 per half-brain, or hemisphere, to defray the costs of collecting, preserving and recording their histories. "It includes all of the vital structures of great interest to PTSD investigators, especially the hippocampus and the amygdala," says Thomas Hyde, Lieber's chief operating officer, referring to parts of the brain linked to emotions and memory.

The brain bank will fuel PTSD research across the nation, with scientists borrowing brain samples for their own work

Researchers will use imaging studies of live brains as a road map. "Certain sections of the brain will show an increased blood flow. Others will show a diminished blood flow," Friedman says. "Certain sections of the brain will be more responsive to certain kinds of chemicals, and vice versa." Animal studies, he adds, reveal "very exciting" alterations in neural connections after extreme stress.

Documenting the response is key, since charting what's going wrong is the first step to fixing it. "Memory, activation of fear circuits and anxiety circuits seem to be overly active in people with PTSD," Hyde says. "If you can understand that chemistry, then you might be able to develop better drugs to treat it."

The brain bank will fuel PTSD research across the nation, with scientists at other institutions borrowing brain samples for their own work. And the bank's benefits could extend well beyond vets: PTSD can affect anyone who experiences trauma, from bad falls to crimes like robbery or home invasion. In fact, many experts believe that the sudden loss of a loved one or an abusive or even negligent childhood can also lead to PTSD. An estimated 6.8% of Americans will suffer from it at some point during their lives.

Those who have experienced PTSD are optimistic about the brain bank's work. Jim Doyle spent 1969 in Vietnam as an Army infantryman and struggled with PTSD for 15 years. "PTSD is real. It's not somebody trying to scam the system. It's not people who are lazy. It's not people who are just doped up," says Doyle, now 65 and living in Fresno, Calif. He's hopeful that the brain bank means that the next generation of soldiers won't need to wage a second war when they come home.

"Maybe they'll be able to find the physical manifestations," Doyle says. "That way, the next guy in the next war won't have to go through years of fighting himself, and everyone around him, because he's not sure what's going on inside his own head." ■