# BRAIN BANKS—PROVIDING PRECIOUS CLUES ABOUT WHY A BRAIN BREAKS DOWN

*A collection of specimens at the Bedford VA is providing insights on Alzheimer's disease and traumatic brain injury*

The brain, running right, is a staggeringly capable instrument—commander of thought and behavior. But degraded by disease or injury, this three-pound organ is associated with some 600 neurological disorders, according to the National Institute of Neurological Disorders and Stroke.

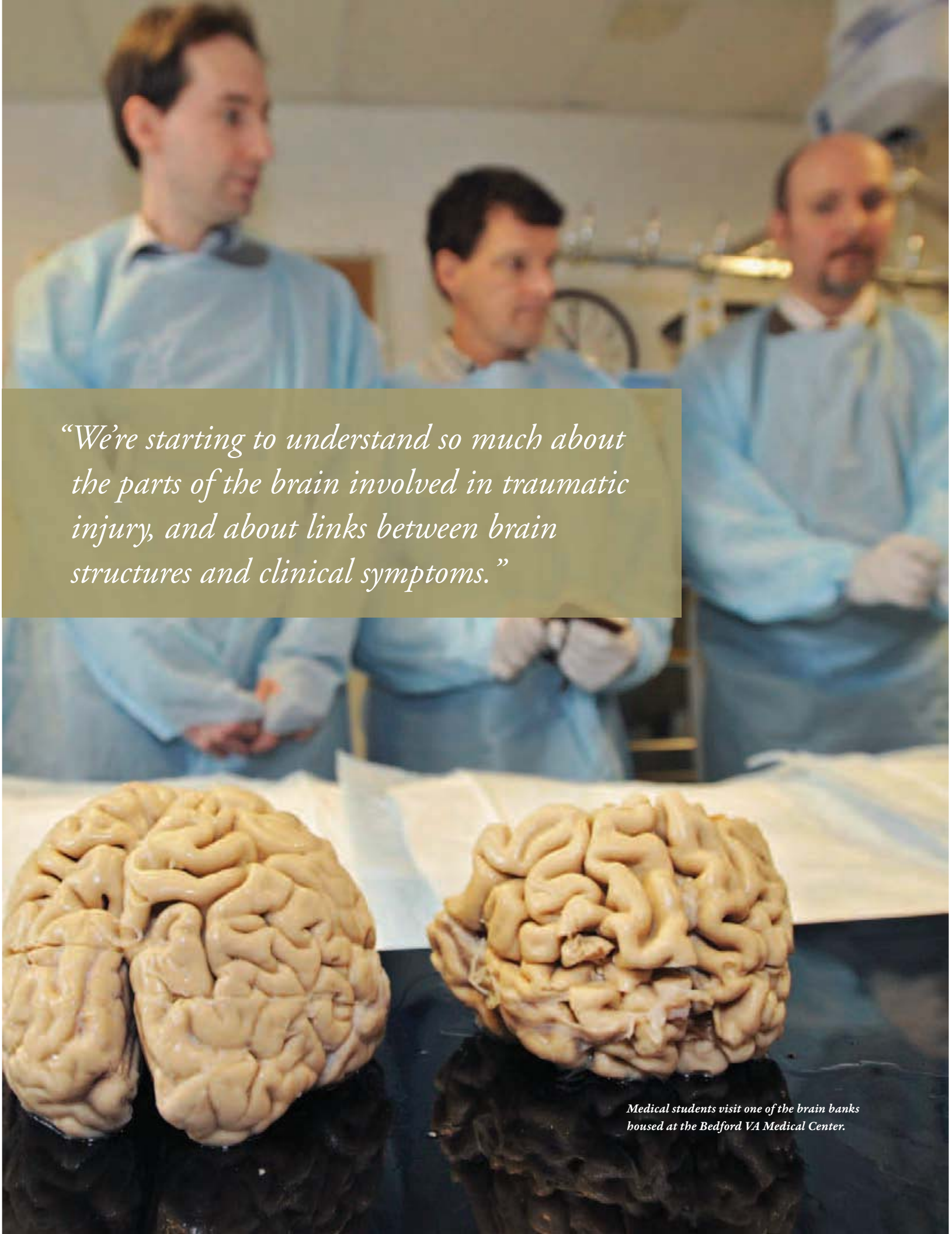
The brain has long kept scientists baffled: What biological changes are to blame in medical conditions such as traumatic brain injury and Alzheimer's disease? Its elaborate structure makes the brain uniquely difficult to study. Also, brain biopsies are too risky, as a rule, and diagnostic images generally fall short of the desired detail. So neurology researchers rely heavily on brain banks, including some housed at the Bedford VA Medical Center in Massachusetts, for collecting clues about the biological nature of brain-related medical conditions. People with these types of diseases—and others without—arrange to donate their brains after death to advance scientists' understanding of the ravages wreaked by various ailments.

"We can't treat what we don't understand," says Ann McKee, MD, head of the neuropathology service for the VA New England Healthcare System and director of the Bedford VA-based brain banks. "The idea with these banks is to learn as much as possible about brain diseases, including their origins and any environmental or genetic triggers."

## Concussions: The sports-military link

At the Boston University Brain Bank at the Bedford VA Hospital, McKee studies the enduring effects of repeated head injury from contact sports and military combat. In the last couple of years, she has focused her investigation on the brains of deceased athletes who received many concussions during their careers—commonly boxers, football players and hockey players. In many of these athletes, researchers have identified a degenerative neurological condition called chronic traumatic encephalopathy, which during life can cause memory loss and erratic behavior.

"We're starting to understand so much about the parts of the brain involved in traumatic injury, and about links between brain structures and clinical symptoms," explains McKee, who is now also studying whether military troops with traumatic brain injury from blasts or other exposures on the battlefield experience the same types of effects. "There are clear parallels with Veterans," notes McKee—chronic traumatic encephalopathy is associated with brain trauma, and exactly how the trauma occurs may not be critical in some of the scientific questions being studied.



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***Medical students visit one of the brain banks housed at the Bedford VA Medical Center.***

McKee believes researchers "are on the brink of a huge breakthrough" in understanding what people go through after a traumatic injury, and that brain banks hold promise, too, for studying mental health conditions such as posttraumatic stress disorder. "We really need to do exactly what we're doing with other conditions—establish a special brain bank to allow us to fully analyze the brains of those who are diagnosed with PTSD," says McKee, who surmises that many people with this "very heterogeneous condition" may have structural brain lesions leading to their symptoms.

To help researchers resolve remaining questions, 29-year-old Iraq Veteran Will Reynolds III has already decided to donate his brain for study after his death. He plans to make the donation through the Sports Legacy Institute, which studies the effects of concussion and often partners in its research with McKee and the Boston University Brain Bank. Reynolds, a West Point alum, was exposed to multiple blasts while serving in Iraq, including an IED explosion that left his left leg and arm severely injured. "Being in my unique scenario, exposed to so many blasts, my brain and other organs may be useful to help Veterans down the line with the same kinds of trauma," he says.

This type of altruistic donation, to spare others suffering, is common, says McKee. "With Veterans, as with athletes, donations are driven by an esprit de corps—'I hope by donating my brain I will help my fellow soldiers in the future.'" In other situations, people want to understand what their family member went through, or if a disease such as Alzheimer's may run in their family.

## How Alzheimer's unfolds

Alzheimer's disease—which affects some 4.5 million Americans, including many aging Veterans, with the figure expected to triple by 2050—is a primary focus of brain bank research along with traumatic brain injury. VA researchers approach the study of Alzheimer's from many perspectives, but the far-reaching role of brain banks in such investigation is hard to overstate, according to Neil Kowall, MD, director of the VA New England Geriatric Research, Education and Clinical Center and the NIH-funded Boston University Alzheimer's Disease Center.

Currently, brain autopsy is the only way to definitively diagnose Alzheimer's disease, Kowall points out. Looking at the brain under a microscope after death is far superior to diagnostic imaging for scrutinizing the telltale brain changes in Alzheimer's: protein clumps called amyloid beta "plaques" and twisted protein fibers called neurofibrillary "tangles."

Animal models have helped scientists understand certain molecular events that the disease involves, but these models' usefulness is extremely limited, says Kowall: "Even between the brain of a monkey and that of a person, there's a massive difference in complexity. They say 'You can't teach an old dog new tricks,' but there's no animal analog to a person not being able to do something that once was easy—balancing a checkbook, or taking apart an engine."

Ruth Henry says difficulty balancing a checkbook was one of the first signs of Alzheimer's disease for her husband, John, who was diagnosed with the condition at age 62 and donated his brain to the Bedford VA, where he received care for several years before his 2004 death. "Math had been a game to John," she says of the post-World War II Army Veteran, who, perhaps ironically, fully embraced the standard recommendations for reducing Alzheimer's risk. He stayed mentally and physically active and ate a healthful

*Research based at the Bedford (Mass.) VA Medical Center is examining the underlying biological damage that may be common to combat troops who survive blasts and football players, boxers and other athletes who sustain head injuries.*

diet. "He just wanted to do whatever he could to help other people avoid what he was going through," Henry says about her husband's reasons for donating his brain for scientific study. John's gift to medical science may be especially valuable to researchers because his identical twin brother, Charles, also contributed his brain after death from a cause unrelated to Alzheimer's disease.

By studying donated brains from those with and without Alzheimer's, says Kowall, VA and other researchers are already homing in on some of the early brain changes in the disease, and how Alzheimer's differs from typical memory loss. "Many people have memory trouble. We are uncovering clues to tell us when mild cognitive impairment is an opening shot of Alzheimer's."

Identifying early changes, Kowall says, could steer scientists toward interventions to halt the progression of Alzheimer's disease before it becomes disabling. "This is a disease without a cure right now. Blocking the early biological processes in Alzheimer's disease requires an understanding of how the dominos fall as the disease unfolds." For understanding how Alzheimer's and other neurological diseases evolve—and in turn, how they might be effectively treated—brain donation is, in Kowall's words, a "unique gift with no adequate substitute."

## Bedford VA houses several brain banks

Dr. Ann McKee of VA and Boston University oversees several brain banks, all housed at the Bedford VA Medical Center. They include those of:

- The Boston University Alzheimer's Disease Center and the school's New England Centenarian Study, the largest and most comprehensive study of centenarians and their families in the world
- The Center for the Study of Traumatic Encephalopathy, a major collaboration with the Sports Legacy Institute that is partly funded by the VA New England Geriatric Research and Clinical Center and several other agencies, including the National Institute on Aging
- The Framingham Heart Study, a project of Boston University and the National Heart, Lung and Blood Institute