The Invisible War on the Brain

Brain trauma from blast force is the signature injury of the Iraq and Afghanistan campaigns, afflicting hundreds of thousands of U.S. combat personnel. Although unseen, the damage strikes deeply into a soldier's mind and psyche.

Marine Cpl. Burness Britt waits to be medevaced out of Afghanistan following an IED strike in June 2011. ANJA NIEDRINGHAUS, AP IMAGES

By Caroline Alexander

INSIDE THE PROTECTIVE BUNKER I waited with the explosives team, fingers wedged firmly in my ears. Outside, shot number 52, trailing a 20-foot length of yellow-and-green-striped detonating cord, was securely taped to the wall of a one-room plywood building with a steel fire door. There was a countdown from five, a low "pow," and a dull thump in the center of my chest. The thump is the hallmark of blast. "You feel the thump," one team member told me. "I've been in blast events where we're actually hundreds or even thousands of feet away, and I still feel that thump."

The mystery of what that thump does had brought me to a World War II bombing range some 40 miles southeast of Denver. Back then it was used to test half-ton ordnance; now it serves to study controlled explosives used by soldiers to blast holes through walls and doors in combat areas—standard practice in modern warfare. The eventual objective of these tests is to discover what that blast thump does to the human brain.

According to the U.S. Department of Defense, between 2001 and 2014 some 230,000 soldiers and veterans were identified as suffering from so-called mild traumatic brain injury (TBI), mostly as a result of exposure to blast events. The variety of symptoms associated with the condition—headache, seizures, motor disorders, sleep disorders, dizziness, visual disturbances, ringing in the ears, mood changes, and cognitive, memory, and speech difficulties—the fact that they resemble symptoms of post-traumatic stress disorder (PTSD), and the fact that exposure to blast events often was not logged in the early years of the campaigns in Afghanistan and Iraq make it impossible to pin down casualty figures.

Despite the prevalence of the condition, the most fundamental questions about it remain unanswered. Not only is there no secure means of diagnosis, but there are also no known ways to prevent it and no cure. Above all, there is

no consensus within the medical community about the nature of blast-induced injury or by what mechanism blast force damages the brain.

BOOM: In the field a single blast event represents a virtually simultaneous amalgam of distinct components, each uniquely damaging. Ignition sparks a chemical reaction, an instantaneous expansion of gases that pushes out a spherical wall of gas and air faster than the speed of sound. This shock wave envelops any object it encounters in a balloon of static pressure. During this fleeting stage—the primary blast effect—the individual does not move. An abrupt fall in pressure follows, creating a vacuum. Then comes the secondary blast effect, a rush of supersonic wind that floods the vacuum, hurling and fragmenting objects it encounters, weaponizing debris as high-speed, penetrating projectiles.

Marines on patrol in Afghanistan in 2009 noticed a motorcyclist pass by, and moments later an IED exploded. “It’s like being kicked by a horse, a horse with a foot that could cover your entire body,” said one survivor of an IED attack. PETER VAN AGTMAEL, MAGNUM PHOTOS

The wind itself causes the tertiary blast effects, lifting human beings or even 15-ton armored vehicles in the air, slamming them against walls, rocks, dusty

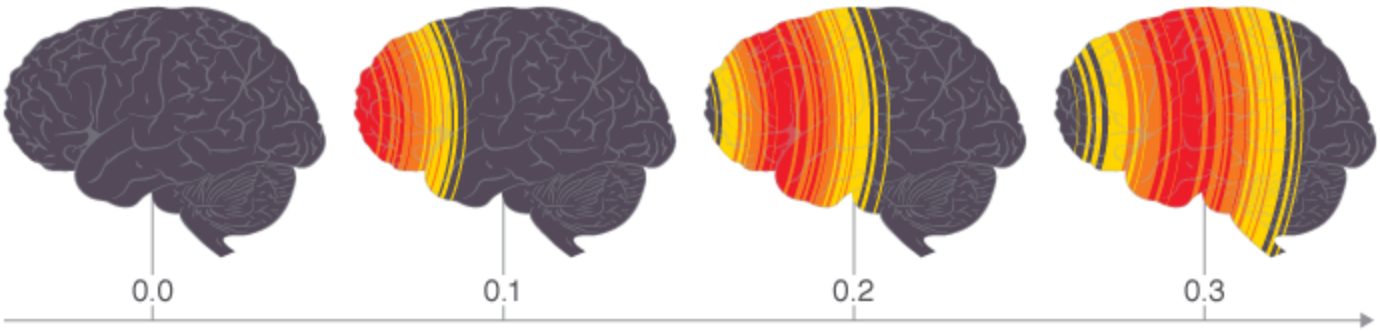
roadsides. The quaternary blast effects are everything else—fire that burns, chemicals that sear, dust that asphyxiates.

The mystery lies in the effects of the primary blast. Theories range wildly: Is it the shock wave's entry to the brain through cranial orifices—eyes, nose, ears, mouth—that causes injury, and if so, how? Or is external shock pressure on the chest channeled inside vasculature up through the neck and into the brain? Does the transmission of complex wave activity by the skull into the semiliquid brain cause an embolism? Does pressure deform the skull, causing it to squeeze the brain? Is the explosive noise damaging? The flash of light? The majority of soldiers diagnosed with blast-induced neurotrauma have also been hurled or rattled by blast wind. Is military neurotrauma, then, simply an exotic form of concussion?

The tests in Colorado arose from a landmark 2008 study by the military of breachers, those soldiers whose job is to set explosives and who for years had been reported to suffer a high incidence of neurological symptoms. The study, conducted by the U.S. Marine Corps Weapons Training Battalion Dynamic Entry School, followed instructors and students over a two-week explosives training course. It turned out that for days after the larger explosions, breachers reported dull aches in the chest and back "like someone had punched them," as well as headaches that "started with shooting pains in the forehead, progressed down the temples, behind the ears, and up through the jaw line."

Blast in the Brain

Studies show that the key mechanical factors associated with brain injury are an increase in intracranial pressure and the brain's motion relative to the skull. The blast wave, or overpressure, affects the brain immediately upon impact with the skull. Pressure in the brain returns to normal after only a few milliseconds, but brain motion can occur for hundreds of milliseconds after impact.



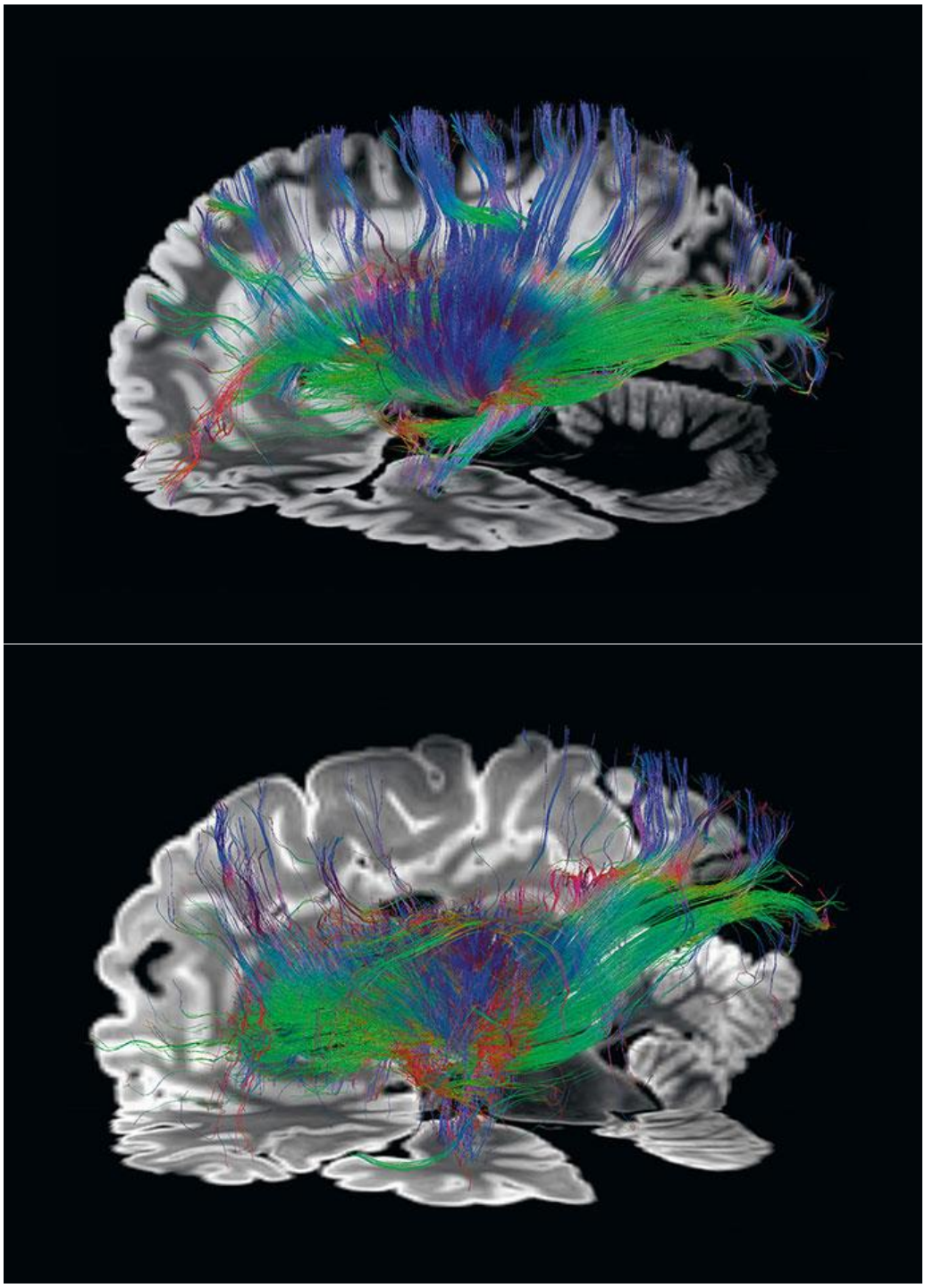
BLAST WAVE TRANSMISSION
in milliseconds

More significantly, neurobehavioral tests administered before and after the course showed a "slight indication of declining performance among the instructors," who typically are exposed to more blast events than students are. This suggested that repetitive exposure even to low-level blasts—even over just a two-week period—could be damaging.

The breacher study went some way toward bringing blast-induced neurotrauma into focus. As Lee Ann Young, one of the study's leaders, noted, it motivated six follow-on research initiatives that continue today. Previously, many in the military and medical communities had found it difficult to believe that a low-energy blast could inflict significant injury. "Our most recent experience was with Gulf War syndrome, where despite many efforts to find consistent threads, we came up mostly dry on specific causes," Col. Christian Macedonia (Ret.), the former medical sciences adviser to the chairman of the Joint Chiefs of Staff, told me. "So there were insane shouting matches in the Pentagon, strange as it may sound now, as to whether blast-related TBI actually existed." In a paper published as recently as 2008, researchers at the Center for Military Psychiatry and Neuroscience Research, Walter Reed Army Institute of Research, concluded that the troubling symptoms were strongly associated with PTSD and that "theoretical concern" about the neurological effects of blast exposure was essentially unfounded.

But today some researchers are floating a different theory: that mild TBI may increase vulnerability to certain psychological disorders, possibly accounting for the high rate of such disorders and even suicide among veterans. Many neurologists now advocate more precise terminology for this signature injury of the recent wars, such as “blast-induced traumatic brain injury” or “blast-induced neurotrauma”—and all I spoke with objected to the qualifier “mild.”

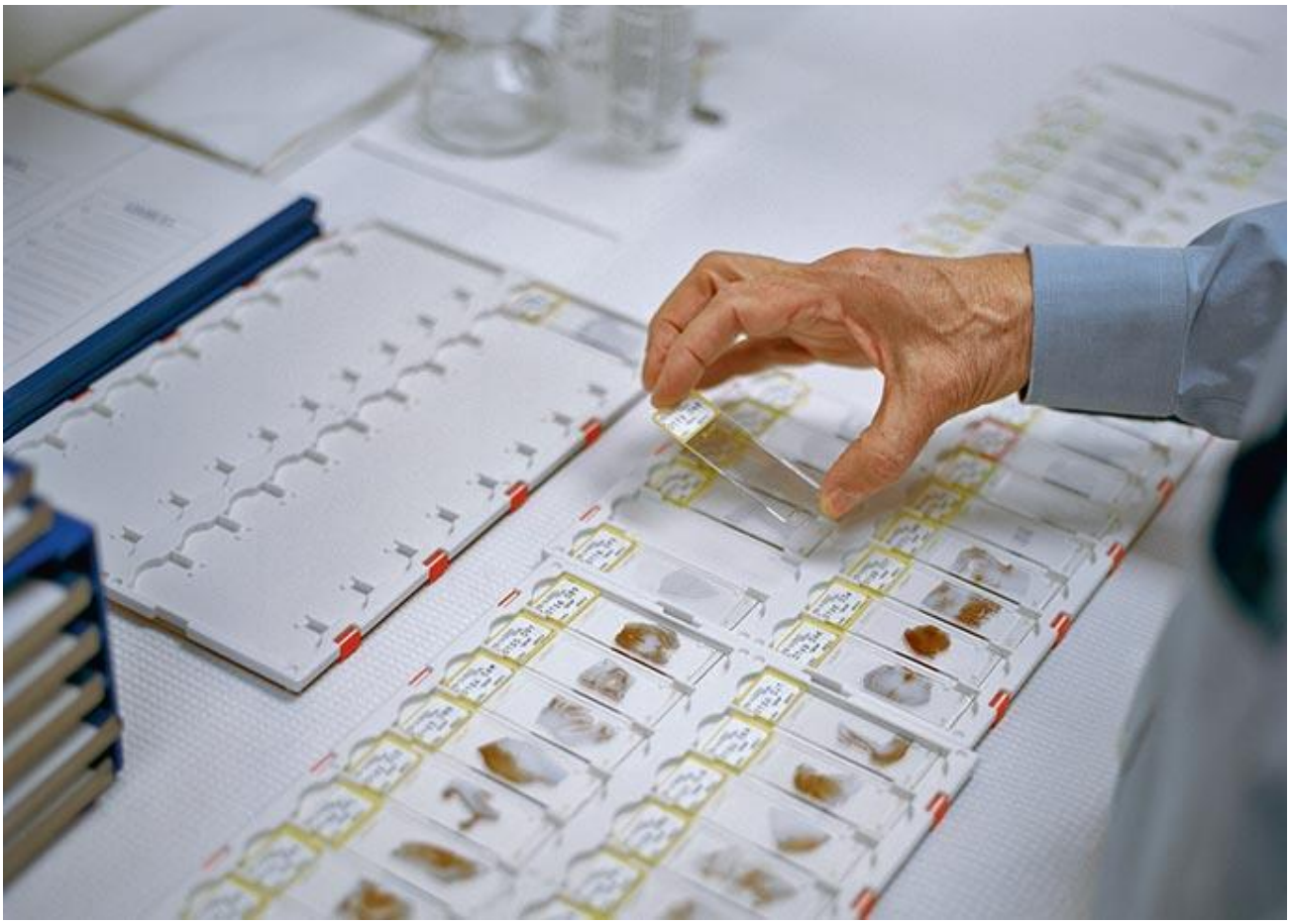
IN THE BUNKER we waited for the smoke to clear, then ventured into still-singed air. The building’s door had been blown off, the opposite wall was in splinters, the struts were broken, and much of the frame was askew. Pressure gauges at head and chest level had recorded the back-blast as it bounced off corners and walls. The explosion itself had been preserved on video, which replayed events, at two to three frames a second, that had flashed by at a speed of 14,000 frames a second—the ignited fuse glowing red-gold in a long, snaking, elegant stem of light, then the gold-black bloom of the explosion: *BOOM*.



Broken Connections

Diffusion tensor imaging tractography dramatically reveals the breakdown of neural connections in the brain of a civilian victim of severe traumatic brain injury (bottom), compared with a healthy brain (top). Researchers in the Military Brain Injury Studies Program at the Uniformed Services University of the Health Sciences plan to similarly map the brains of deceased veterans of recent campaigns to assess blast effects. Slides of delicate brain

tissue (below) hold crucial clues. “I think I know what blast force does to the human brain,” says program director Daniel Perl. IMAGES (TOP) COURTESY BRIAN L. EDLOW, MASSACHUSETTS GENERAL HOSPITAL; REPRODUCED WITH PERMISSION FROM THE *JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY*



Shot 52 was one of a series intended to cast light on the phenomenon of back-blast, the reflection of blast pressure off a surface. Other studies are examining the length of blast exposure and the frequency and type of blast. On site to lead the analysis was Charles Needham, a world authority on blast physics. Studying a computer-generated graph, he traced the spikes and dips of pressure that oscillated through five cycles before flattening out. The entire sequence lasted some 65 milliseconds. One hundred milliseconds is the minimum time it takes for a human to react to any stimulus—it had taken less than five milliseconds for the shock wave to hit the gauges on the walls. As Needham pointed out, “Anywhere in that room—it’s on you.”

Fatherly in manner, with white hair and a full white beard, Needham had been described to me by a colleague as a "cross between Santa Claus and Eeyore," an impression that belied his stature as a high wizard in the black art of explosives. With degrees in physics and astrophysics, he is an authority on modeling all variety of blast events and the dynamics of blast reflection, and he spoke with wistful nostalgia of the big "rumble booms" of high-ordnance tests of years past. A glance at his résumé calls attention to the diversity and sheer spookiness of blast-related issues: "modifications to fireball behavior," "high explosive simulation of nuclear effects," and "Shock and Vibration symposia."

Needham's objective was to provide breachers with maps that would show which areas of a given type of structure are safest from reflected pressure. How a blast is reflected is determined not only by whether a space is square or rectangular, and the ceiling high or low, but also by where the wall studs lie, the number and placement of doors and windows, whether there are gaps or holes in the enclosure, whether there is furniture in the room. A shock wave bouncing off a rigid surface, whether of thin plaster or of steel, can be more powerful than the original wave. (Notoriously, the back-blast reflected off the ground at Hiroshima was more powerful than the actual explosion.) The corners of a room, where one might instinctively seek shelter, are particularly dangerous—as is being the third man in a line of breachers carrying protective shields, which, as it turns out, also reflect shock waves. A blast even reflects from within a soldier's helmet to his head. Every feature in a landscape, every gesture a person makes, shapes a blast event.

A terse conclusion of the original 2008 breacher injury study cited "clear evidence" that recommended safe standoff distances required revision. "We … found errors of more than a factor of two in some of those training manuals," Needham said, referring to breacher instructions: As a result, the manuals were modified in 2012. Encompassing a multitude of variables, calculations

about blast events are elaborately difficult, and only in recent years has it been possible to make the kind of models Needham is now devising. “These are large calculations and take a lot of computer time,” he said. Or, as another blast authority put it, “Until very recently, the dominant force that caused all this damage was basically magic.”

KEEN INTEREST IN BLAST effects began in World War I, when the signature mechanism of injury was—as in the wars in Iraq and Afghanistan—blast force, mostly in the form of exploding artillery shells. The term “shell shock” first appeared in February 1915 in an article in the *Lancet* that examined the case studies of three British soldiers exposed to blast events who complained of sleeplessness, reduced visual field, and loss of taste, hearing, and memory. Initially their affliction was believed to be a “commotional disorder,” referring to agitation of the brain caused by a blast shock wave. A leading theory was that the shock wave traveled to the brain through spinal fluid.

The shock wave from a distant explosion “felt like it lifted my innards and put them back down.”

—Kevin Parker

But as the war continued, the condition was attributed to weakness of nerves, given the fact that many men appeared to be otherwise uninjured. The term “shell shock,” implying that the shell burst itself was the cause of the damage, fell out of favor. The revision of diagnosis had profound consequences. In the following decades the shell-shocked soldier came to symbolize the emotional damage that is the cost of war, and medical research ceased to investigate the possibility that blast-force injury might be physical. “When I was in medical school, we were told about shell shock in World War I,

that people then believed the brain could be damaged by blast waves from exploding shells," Colonel Macedonia said. "It was told as a story about how ignorant the medical profession was a hundred years ago."

The shell-shocked soldiers of that war can be tracked through British Ministry of Pension files into the 1920s, '30s, '40s, and beyond. Case reports give details of veterans sunk in lethargy or melancholy, "muddled" in thought, shaking convulsively on street corners, or going "around the bend" and exploding in paranoid acts of anger. Growing up in England, my parents knew of men whom they were told had "been 'funny' since the war." These reports represent the best data available on the long-term fate of the shell-shocked veteran.

After World War II, in 1951, the U.S. Atomic Energy Commission created the Blast Biology Program to test on various animals very large explosions that simulated the effects of nuclear events. Oxen, sheep, pigs, goats, dogs, cats, monkeys, rats, hamsters, rabbits, mice, and guinea pigs were subjected to live blasts or placed in shock tubes. (A shock tube is a long tube fitted with an internal membrane through which pressurized air bursts. This lab simulation, stripped of heat, debris, chemical fallout, and back-blast variables, creates a "pure" blast shock wave.) In the early 1980s the focus of research shifted from nuclear blasts to the low-level explosives characteristic of today's war theaters.

"MOST OF OUR MEDICAL research on blast injuries was either on fragmentation wounds or what happens in gas-filled organs—everyone was always concerned in a thermonuclear explosion what happened to your lungs and your gastrointestinal tract," Lt. Col. Kevin "Kit" Parker, the Tarr Family Professor of Bioengineering and Applied Physics at Harvard, told me. "We completely overlooked the brain. Today the enemy has developed a weapon system that is targeted toward our scientific weak spot."

Parker, a towering figure with a shaved head and booming voice, is also a former U.S. Army infantry officer who served two tours in Afghanistan, where he saw and felt the effects of blast force. “There was a flash in the sky, and I turned back toward the mountains where the fighting was,” Parker said, recalling the day in January 2003 when, in the hills of Kandahar, the shock wave from a distant explosion passed through his body. “It just felt like it lifted my innards and put them back down.”

Mostly he was made aware of the range of damage blast inflicted. “When bombs are going off, it’s easier to forget about the guy who’s been a little out of sorts than the guy who’s sitting near him and got both his legs blown off,” Parker said. “But the guy who’s going to have the more serious long-term issues probably is going to be the guy who had the brain injury.”

In 2005 Parker, who was then involved in cardiac tissue engineering, turned his attention to blast-induced neurotrauma. He began by reviewing the science for a class of proteins—integrins—that transmit mechanical forces into cells. Using specially designed magnetic tweezers and a device resembling a miniature jackhammer to simulate the abrupt stretching and high-velocity compression of blast effects, Parker and a small team of students subjected engineered tissues of rat neurons, or nerve cells, to blastlike assault. The integrins on the cell surface initiated a cascade of effects culminating in a dramatic retraction of axons, the long tendrils that serve as a neuron’s signaling mechanism.

By working at the cellular level, Parker’s team sidestepped two central difficulties of any blast research—namely, that one cannot expose humans to blast events and that animals are poor substitutes for humans. On the other hand, results from cells in a petri dish cannot be extrapolated to a human being.

THE ARRAY OF THEORIES neurologists are actively pursuing stands as eloquent testimony to how wide open blast-induced neurotrauma research is. Lee Goldstein, of Boston University School of Medicine, has taken a very different approach. “People focus on the pressure wave,” Goldstein told me. “What’s behind it is the wind.” Goldstein’s range of expertise can be read in his full title: associate professor of psychiatry, neurology, ophthalmology, pathology and laboratory medicine, and biomedical, computer, and electrical engineering. At 52, he has the lean build, long dark hair and beard, and intensity of purpose of a desert prophet.

In May 2012 he published the results of studies that examined a possible association between blast-induced neurotrauma and chronic traumatic encephalopathy (CTE), a neurodegenerative disease that he and his team discovered in the autopsied brains of four military veterans with blast exposure. Goldstein’s co-author, Ann McKee, of VA Boston, had been studying CTE in the autopsied brains of football players and other athletes. First reported as a “punch drunk” syndrome in boxers in 1928, CTE is associated with athletes who sustain repetitive head trauma. An incurable and ultimately fatal neurodegenerative disease, CTE leads to cognitive disability and dementia. The disease can be detected only at autopsy and is revealed by abnormal tangles of a protein called tau.

To test the theory that blast exposure may have triggered CTE pathology, Goldstein’s team exposed mice to a single shock-tube blast that simulated the effects of a moderate-size explosive. High-speed cameras captured the results—a rapid bobble-head effect, as the heads of the mice shook back and forth in reaction to the force. In 30 milliseconds, far less than the blink of an eye, the oscillating wind had spiked and dipped nine times. “In one blast you’re really getting multiple hits,” Goldstein said. “So it’s like you’re packing a whole bunch of hits into a very short time.”

Two weeks after exposure to the blast, the mice brains showed an accumulation of chemically modified tau protein and other damage. Critics of the study, however, point out that three of the four human cases that inspired the shock-tube experiments had experienced additional trauma unrelated to blast and that tests on mannequin models indicated that the bobble-head effect was not usual in the field.

Some researchers believe that it's a mistake to focus only on the head. "The whole body is exposed to huge kinetic energy," said Ibolja Cernak, describing the impact of a blast event. "Athletes do not have this kind of whole body exposure." The chair of Canadian military and veterans' clinical rehabilitation research at the University of Alberta, Cernak began her research on the battlefields of Kosovo, when she noticed that some soldiers and civilians exposed to blast exhibited symptoms reminiscent of certain neurodegenerative diseases. The blast pressure wave hits the chest and abdomen "like a huge fist," Cernak says, transferring its kinetic energy to the body. "That kinetic energy generates oscillating pressure waves in the blood, which serves as a perfect medium to further transfer that kinetic energy to all organs, including the brain."

Experiments she conducted on mice revealed that inflammation occurred in the brain whether the head had been protected from blast or not—inflammation, she argues, that starts a process of damage comparable to that seen in Alzheimer's disease. By contrast, protection of the thorax significantly reduced inflammation in the brain, suggesting that the blast-body interaction has a crucial role in blast-induced brain injury.

AS OF NOW, the only wholly reliable method of directly examining the biological effects of blast force on the human brain is autopsy. In 2013 the Department of Defense established a brain tissue repository to advance the study of blast-induced neurotrauma in service members. Overseen by Daniel

Perl, professor of pathology at the Uniformed Services University of the Health Sciences, in Bethesda, Maryland, the repository has been receiving brains donated by service members' families. This has allowed researchers, Perl says, to get "to the tissue level to really see what's going on." As he points out, magnetic resonance imaging (MRI) of the living brain has a resolution a thousand times less than what can be seen when the brain is examined under a microscope.

Perl's expertise extends from work on CTE, Alzheimer's, and other age-related neurodegenerative diseases to research on a unique complex of neurological disorders in a small population in Guam (a mystery described in Oliver Sacks's popular book *The Island of the Colorblind*). Perl has also written of shell shock and its relationship to modern blast-induced brain injuries, noting that despite a hundred years' use of explosive force in warfare, there have been "no detailed neuropathology studies ... in the human brain after blast exposure."

Now, 18 months into the brain tissue study, Perl said he's seeing revelatory results. "We believe we're getting close to identifying unique changes in the brains of blast-exposed soldiers that are not seen in brain injuries of civilians," he said, referring to common blunt-force trauma such as athletes sustain. "What we're seeing appears to be unique to blast. This is an injury that appears to be unique to military experience."

If he's correct, the findings will have major implications not only for treatment but also for diagnosis and prevention. "I think we'll have to sit down with the helmet-design people and the body-armor people," he predicted. "A lot of designs were based on very different assumptions."

For living soldiers, meanwhile, reliable methods of diagnosis remain tragically elusive. In June 2011 the *New England Journal of*

Medicine published the results of a study that for the first time succeeded in detecting structural abnormalities in the brains of blast-exposed soldiers by using an advanced form of MRI. Although hailed as a landmark in an accompanying editorial, the paper was weakened by the fact that every participant had also experienced other traumas, such as being struck by a blunt object or being in a motor vehicle crash.

READ MORE:

Behind the Mask

Blast injury to the brain changes soldiers in ways many can't articulate; some use art therapy to reveal themselves. Body armor can stop shrapnel, but nothing can stop blast waves.

A number of studies investigating possible biomarkers may have findings that will aid future diagnosis: A blood test for unique protein markers indicative of brain cell damage has proved promising, for example, and is now being tested

by the military. (It is effective only if administered within a few days of the injury.) And in 2014 a small study of 52 veterans successfully used an MRI technique called macromolecular proton fraction (MPF) mapping, which examines levels of myelin, a major component of brain white matter; MPF mapping has been used to study patients with multiple sclerosis, who have reduced levels of myelin, the fatty sheathing that protects and insulates neurons. Evidence of brain white-matter damage was detected in 34 veterans with exposure to one or more blast events, compared with 18 veterans without blast exposure.

“We’d told the veterans to give us their best estimates of how many blast-related mild traumatic brain injuries they had sustained during their military careers,” said Eric Petrie, a professor of psychiatry at the University of Washington and the lead author of the study. “But how accurately can veterans recall these events? Some in the study were five to six years out from the time of their last blast exposure,” he said, summing up one of the fundamental problems of all diagnostic studies that depend on self-reporting. In the future, photonic crystalline materials that change color when exposed to blast waves, worn as stickers on uniforms and helmets, may provide an objective measurement of blast exposure.

Despite the array of promising strategies, for the time being diagnosis still depends, as it did in WWI, on clinical assessment, which may now involve computer-administered examinations such as the Automated Neuropsychological Assessment Metrics: “Did you experience any of the following: Dazed, confused, saw stars? How much does this word describe how you feel? ‘Shaky.’ ”

COMPLEX AS IT MAY BE, a blast event can be created for very little money and with minimal expertise. Explosively formed penetrators, a type of IED used to pierce armored vehicles, can be assembled for a few dollars. Disks that become

bullet-shaped and molten hot as they fly through the air, these explosive projectiles can, in the words of one ordnance expert, cut through an armored car "like a hot butter knife." In this way 25 dollars' worth of technology can take out a million-dollar armored vehicle and kill or inflict grievous injury on the soldiers in it. The cost of their medical care—possibly over decades—will add significantly to the economic disparity. Given this cost-effectiveness, explosive force is likely to remain a signature weapon of modern warfare.

Today, while researchers strive to figure out what goes on when blast force encounters the human brain, untold numbers of soldiers are struggling with the aftermath of their own encounters.

BOOM. On patrol in Iraq in 2009, Robert Anetz felt the immense pressure against his body. Then everything went numb. "Everybody started shouting, 'Are you good? Are you good?' You check for blood," Anetz said. There was no blood, so he thought he was good. But seven months after returning from Iraq, he had a seizure while driving, and a grand mal seizure six months after that. Now rebuilding his life as a student and volunteer firefighter, his daunting regimen of 15 different medications is down to three, but the headaches and migraines have not gone away.

Enrique Trevino, who at the age of 21 survived a massive IED ambush in Afghanistan one night two weeks before he was to return home, remembers only the bright flash and his buddies screaming his name. "I'll never forget that flash," he said. "It almost looked like a lightning strike." When he finally awoke in Fort Hood, Texas, he learned the explosion that had knocked out his night optics had also knocked out his power of speech and his peripheral vision. He now works to rebuild his mind with mental tasks like counting backward from 50, but he suffers daily from migraines and nightly from his dreams.

About a year after his return home, Trevino said, “it all came crashing down on me.” He survived a suicide attempt. A friend of his who had also served in Afghanistan did not. “They found him in his home,” Trevino said. “He, he—nobody would have ever thought—nobody would have ever been—nobody ever, nobody, no one, nobody saw that. Nobody saw.”

And nobody saw it for my brother-in-law, Ron Haskins, from whom I first learned about breachers. After retiring from the Army Special Forces, he worked with a private security force in Iraq. He sustained two IED attacks that left him with headaches and ringing in his ears so loud he was unable to sleep. On his return to the United States, he worked for the Department of Homeland Security and conducted breacher training courses for a security company of his own. One night in the summer of 2011, for reasons no one could fathom, he picked up a gun and ended his life.

“We should get you guys to come out to New Mexico so you can see the devices, have explosions go off,” Ron had told me about a training course he led. “You’ll be half a mile away, and you’ll be amazed at how a couple of pounds will rattle the earth around you.” □