By Jen Guidera

“Improvised explosive devices (IEDs), roadside bombs and grenades pose a serious risk to soldiers in Iraq and Afghanistan. Not only do these explosive devices threaten the lives of soldiers, but they can also cause irreversible brain damage. Referred to as blast induced mild traumatic brain injury (bTBI), brain damage caused by explosions is a widespread problem for soldiers in Iraq and Afghanistan. The United States Army estimates that as many as 20% of returning soldiers from Iraq and Afghanistan suffer from bTBI (1). At the Walter Reed Army Medical Center, 59% of soldiers who came in for a routine check up between 2003 and 2005 were found to have bTBI, and in more than half of these cases, the brain damage was severe. For this reason, traumatic brain injury is often referred to as the signature wound of the Iraq and Afghanistan wars (2).

Despite the prevalence of bTBI in soldiers, the specific way in which explosions damage the brain is not fully understood. For this reason, diagnosing bTBI is difficult and even today, current neuroimaging is not always successful in detecting bTBI immediately following injury. In the past, bTBI was often underreported or misdiagnosed in veterans. Returning veterans that exhibited memory loss, headaches, anxiety, depression, or confusion were often thought to have post-traumatic stress disorder—psychological damage that results from a traumatic experience (3). Some of these soldiers may have suffered instead from traumatic brain injury, a fundamentally different ailment, which unfortunately has limited treatment options (4). A better understanding of how explosive forces translate into brain damage is necessary to better diagnose and treat bTBI in our veterans.

In addition to its prevalence, blast induced traumatic brain injury poses an urgent problem because its symptoms..."
are often devastating and permanent. Veterans with bTBI often exhibit memory loss, seizures, poor attention, decreased cognitive functioning, and depression (5). According to the Brain Trauma Foundation, traumatic brain injury increases the risk of acquiring Alzheimer’s disease by up to 400 percent (6). The wide range of symptoms of bTBI results from the fact that damage often occurs throughout the brain, rather than solely at a specific area. This pervasive brain damage manifests as diffuse axonal injury, and is present in around half of severe brain injuries (7).

A Veteran brings Experience on the Battlefield into the Lab

Although many studies have established the link between non-invasive explosions and bTBI, scientists did not understand the unique way in which explosions damage the brain until recently. One previous theory postulated that the blast waves created extra gaps, known as pores, in the membrane of neurons. According to this theory, ions would flow through the pores and disturb the delicate chemical equilibrium of the neurons (8). However, the influx of ions does not explain the large-scale damage characteristic of bTBI. For example, explosions often lead to the retraction of axons, the projections of neurons that carry information in electrical impulses and are crucial for proper neural functioning. Though an influx of ions may explain local damage, it does not account for the retraction of axons throughout the brain (9).

This year, one army veteran changed scientific understanding of bTBI by exploring how explosions affect the brain. After serving overseas, Harvard researcher Kevin Kit Parker assembled a team of Harvard bioengineers to study diffuse axonal injury, the type of brain damage often seen in soldiers with bTBI. Parker’s first hand experience in Afghanistan motivated his research. In an interview with ScienceNOW, Parker explained, “I kept seeing buddies of mine get hit and thought, ‘All right, I’ll take a look at this’”(10).

Before serving in the military, Parker’s research focused on engineering cardiac tissue. Although his research changed focus when he returned from Afghanistan, Parker was able to apply his experience in the field of tissue engineering to the problem of traumatic brain injury. In order to observe the effects of explosions on brain tissue, Parker grew neonatal rat cortical neurons, cultured over a period of five days (9). Parker’s engineering background was also of use in building machines specifically designed to stress the rat neurons. In an interview for The Science Network, Parker emphasized the importance of engineering new techniques to understand bTBI, stressing, “we need to build in vitro experimental models to understand brain injury.” (11)

Two Systems to Model the Explosive Force

While previous studies were often limited to observing bTBI in past veterans, Parker utilized technology to replicate bTBI in real time (2). Parker and his team modeled the forces of an explosion on the brain in two ways. First, the team designed and built a high speed stretcher (HSS) system to mimic the abrupt and non-constant force of an explosion wave. The high speed stretcher system consisted of a stretchable platform and a clamp to keep the cultured tissue in place. Entire sheets of tissue were placed on the platform and subjected to quick, abrupt strains meant to mimic the force of an explosion. The high speed stretcher system consisted of a stretchable platform and a clamp to keep the cultured tissue in place. Entire sheets of tissue were placed on the platform and subjected to quick, abrupt strains meant to mimic the force of an explosion. Secondly, the team used magnetic tweezers to strain individual neurons. Magnetic beads were attached to the neurons, creating an attractive force between the neurons and the tweezers. The magnetic tweezers could then be used to subject the individual neurons to forces of varying degrees (9).
Explosive Results

Never before had scientists so closely observed the mechanism through which explosive forces damage the brain. The team’s most important discovery was that integrins play a large part in the pervasive brain damage resulting from explosions. Integrins are proteins contained in the cell membrane that allow the inside of the cell to respond to outside forces. Beginning with the perturbation of the integrins, the force of an explosion triggers a devastating cascade of intracellular reactions, eventually leading to the retraction of axons. Since axons are vital for the communication of neurons, the collapse of these pathways severely compromises the functionality of the brain (9).

The study’s results also suggest that membrane poration, which was previously thought to be a cause of bTBI, does not account for the characteristic pervasive brain damage. In Parker’s study, neurons subjected to strain by the magnetic tweezers exhibited axonal damage even when membrane poration was not observed. This outcome suggests that another neuronal mechanism is responsible for bTBI—most likely faulty integrin signaling (9).

Importantly, the results of Parker’s study show that the damage caused by an explosion can be slowed. Using the high speed stretcher system, groups of neurons were subjected to a blast-like force. Inhibitor HA-1077 was immediately added in order to prevent the faulty integrin signal cascade. Focal swelling, a measure of damage to the axons, decreased proportionally with the addition of the inhibitor, suggesting the inhibitor’s potential to mitigate explosion-induced axonal damage (9).

Past, Present and Future Soldiers

Parker’s findings have positive implications for current soldiers and past veterans. Previously, bTBI was often under diagnosed or mistaken for posttraumatic stress disorder (PTSD) (3). A better understanding of bTBI may improve diagnostic techniques and lay the groundwork for research on possible treatments for bTBI.

Future soldiers may also benefit from Parker’s findings. The helmets that soldiers wear today are designed to protect against direct blunt force from shrapnel or roadside bombs, but not necessarily the non-invasive force of an explosion (2). Parker’s findings afford a better understanding of exactly how explosive forces translate into brain damage, providing the basis for future research on novel combat gear. Furthermore, Parker’s study suggests that brain damage can be slowed using an inhibitor to prevent the cascade of faulty signals (9). Scientists might be able to incorporate this inhibitor into immediate treatment for bTBI, since studies show that axonal damage takes hours or days to reach full effect.

Until we understand more about bTBI, the non-invasive force of roadside bombs, grenades, and improvised explosive devices (IEDs) will remain a serious threat to our soldiers. No one knows this better than Kevin Kit Parker, himself an Afghanistan veteran. By fusing his experience on the battlefield with his prowess in the lab, Parker is improving our previously limited understanding of bTBI. His study is an important step toward protecting the most valuable yet least understood organ for our soldiers—the human brain.

References
1. G. Zoroya, “Study: Up to 20% of Troops may have TBI,” Armytimes, 2008.

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