



## Afghan Tragedy Renews Focus on Head Trauma in Soldiers

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It's the signature injury of the Iraq and Afghanistan wars -- mild traumatic brain injury -- and it's caused most often by the signature weapon of those wars, the improvised explosive device (IED).

Because of major advances in medical care in the field, coupled with better protective armor, soldiers for the first time are surviving close-proximity bomb blasts in large numbers. But only now are researchers beginning to understand the nature of these injuries, as well as the long-term implications for physical and psychological health.

An estimated 16% to 18% of the more than two million U.S. troops deployed in Iraq and Afghanistan since 2001 may have been affected.

Soldiers' brain injuries are now receiving extra scrutiny with the case of Army Staff Sgt. Robert Bales, accused in the March 11 shooting rampage in Afghanistan's Kandahar province that left 16 civilians dead in their homes. Bales had reportedly suffered a concussion during a 2010 deployment in Iraq when his vehicle rolled over.

### The Injury

IED explosions produce high-velocity shock waves, and a person in the path of these "overpressure" waves can experience multiple effects including bleeding in the lungs and disruptions to internal organs.

Multiple mechanisms contribute to blast injuries. In most cases, the primary shock wave injury is accompanied by blunt trauma when the recipient's head hits a wall or the roof of a vehicle. There also may be penetrating or thermal injuries.

The nature of the primary supersonic wave injury remains controversial, according to Alisa Gean, MD, a neuroradiologist at the University of California San Francisco.

Some researchers have suggested that the wave force directly enters the brain parenchyma through the eyes and ears, while others believe that the blast force causes deformation of the skull.

"The skull is not as rigid as people think. Bone is a living substance, and when it flexes it can cause stresses and strains on the parenchyma," Gean told MedPage Today.

Deformation of the brain further triggers changes in cortical cells, resulting in abnormalities in electrical activity, metabolism, and damage to the interconnecting axons, explained Christopher Giza, MD, of the University of California Los Angeles.

Accompanying injuries, such as to the lung, liver, and kidney, also can contribute by failing to provide optimal blood flow and quality needed for the injured brain.

"Normal function of the brain requires tremendous energy, almost 20% to 25% of the body's total energy," Giza explained.

An additional contributing factor can be acceleration-deceleration damage when the brain strikes the skull, he added. The result can be a person who reports feeling hazy or confused and has trouble focusing or remembering, similar to what is often seen with head-injured athletes.

Patients sometimes report migraine-like headaches, but they can also appear normal and may not even realize they have been injured.

The rash of stories about former soldiers showing severe and even catastrophic sequelae -- epitomized by the Kandahar massacre -- has created an intense focus on this problem, similar to the publicity surrounding repetitive concussive injuries in football players.

For athletes, the outcry has begun to result in changes in rules and the game culture, as well as requirements for remaining out of play for specific periods of time.

But the situation is much more complex in combat, where the acute stress of danger can contribute to confusion following an injury. In addition, soldiers may be unwilling to acknowledge invisible injuries, and they may have to remain in harm's way for hours or even days.

#### Looking for Evidence

To date, experts have not even been able to clearly define mild traumatic brain injury, or concussion. The usual way of assessing the injury today is according to the individual's level of consciousness, ranging from coma in severe injury to drowsiness in moderate injury, and awake but incompletely focused or confused in mild injury.

Many groups have tried to formulate diagnostic criteria, but most efforts have been criticized as lacking in specificity for the combat environment.

What is needed is an objective way of assessing these individuals, which can then be used for diagnosis and treatment, and for determining fitness to return to duty, according to Jam Ghajar, MD, PhD, president of the Brain Trauma Foundation and a neurosurgeon at Weill Cornell Medical Center in New York City.

The foundation is collaborating with the CDC to meet this need, with funding from the Defense Health Program.

"We are working toward an evidence-based definition of mild traumatic brain injury that can be used to rule concussion in or out based on objective measures," said Ghajar, who is principal investigator for the initiative.

Representatives of the Department of Defense, Veterans Affairs Department, National Institutes of Health, and various medical societies are participating in the program, which is expected to complete its work by September 2013.

"On this definition will hinge diagnosis and treatment," Ghajar told MedPage Today.

Symptoms also will be incorporated, but will be tied to results of objective measures such as tests of balance, attention, and memory that are best performed before deployment and again at the time of head injury to assess changes.

Current approaches to testing have been criticized, with reports by the ProPublica news organization questioning the accuracy of the screening test known as the Automated Neuropsychological Assessment Metrics and advocating more reliable tests and wider use of new technologies such as bloodstream biomarkers of injury and improved imaging techniques.

Even the term "mild" brain injury has shortcomings and is overly simplistic, argues Gean, who is also affiliated with the Brain and Spinal Injury Center at San Francisco General Hospital.

"When individuals have lost their marriage, their job, their health, and even their whole outlook on life, that doesn't define 'mild' to me," she said.

#### The PTSD Link

In 2008, researchers from the Walter Reed Army Institute reported on a survey of more than 2,500 members of the Army infantry, and found that almost 5% had experienced a head injury associated with a loss of consciousness, while 10.3% reported having an injury with changes in mental status but without actual loss of consciousness.

When the researchers compared soldiers who reported mild traumatic brain injuries with those with other types of injuries, they found that head injuries were more common with blast events, multiple exposures to explosions, and hospitalizations.

These researchers also identified a strong link between traumatic brain injury and PTSD, with 43.9% of those who had lost consciousness and 27.3% of those with mental status changes later showing characteristics of PTSD, compared with 16.2% of those whose injuries did not involve the head.

As to how concussion could contribute to PTSD, they noted that multiple mechanisms may be involved. These included "biologic processes associated with exposure to extreme stress, activation of the hypothalamic-pituitary-adrenal axis, autonomic reactivity, reactive cell-mediated immune responses, disturbed sleep physiology, and altered perceptions of symptoms," wrote Charles W. Hoge, MD, and colleagues in the *New England Journal of Medicine*.

Other researchers have identified brain abnormalities on imaging studies of PTSD patients in areas of the brain associated with hypervigilance such as the amygdala. Paradoxically, it appears that patients who had milder injuries can have worse PTSD symptoms, according to Gean, who spent two tours attending to head-injured soldiers in Landstuhl, Germany, where the wounded from Iraq and Afghanistan are sent. She believes that the worse symptoms reported by soldiers with milder head trauma may be explained by the fact that they actually remember the trauma "and relive the horrific nightmare they went through."

#### Exploring the Mechanisms

Considerable attention is now being paid to the effects of brain injury at the cellular and molecular levels. One group of researchers from Harvard University has conducted a series of in vitro experiments in which they mimicked trauma to rat cortical neurons. They found that the trauma disturbed the functioning of neuronal integrins, which help maintain plasticity in synapses, and led to swelling of the neurons as occurs in diffuse axonal injury in vivo. Integrins also appear to be "key players in memory and learning," the researchers explained in the open-access journal *PLoS One*.

Sophisticated imaging techniques such as functional MRI and diffusion tensor imaging also will help in understanding these injuries -- for example, by revealing petechial microhemorrhages -- although more research is needed to fully establish what normal brain structures look like with these technologies.

Meanwhile, the main practical focus remains on preventing a second injury in soldiers and civilians alike, according to UCLA neuroscientist Giza, because the brain is resilient and may recover if it is protected through limited activity and rest.