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Helping Our Heroes: Investigating Blast Induced Neurotrauma in U.S. Troops

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Helping our Heroes

Investigating blast induced neurotrauma in U.S. troops

By Amy Oprean

From the machine guns and air raids of the World Wars to the lingering effects of Agent Orange in Vietnam, the threats that U.S. troops endure have continually changed with every era of war. No exception to this rule are the conflicts of Afghanistan and Iraq, which are the first in U.S. history to see improvised explosive devices (IEDs) – bombs detonated under artillery vehicles and on crowded streets, sometimes strapped to suicide bombers – as the primary mode of attack waged on U.S. soldiers. Young in their diagnosis but vast in impact, blast injuries from IEDs make up about 80 percent of injuries to U.S. troops returning from Iraq, and have earned the title *the signature injury* of these wars.

The prevalence of injuries from this weapon of choice has elicited an onslaught of questions that researchers are scrambling to answer: What are the long term effects of these close-range, frequent blasts? How do blast waves impact soldiers in artillery vehicles differently than those on foot? And perhaps the most perplexing, how are these blasts causing traumatic brain injury, or TBI, in 10 to 20 percent of returning troops?

Wayne State researchers, Dr. Cynthia Bir and Dr. Pamela VandeVord, and a team of collaborators are working to answer those questions with the project *Blast Induced Neurotrauma,* an investigation funded by a $790,000 grant from the Office of Naval Research and additional funding from the Department of Veterans Affairs. Using a state of the art blast tube – one of less than a dozen owned by U.S. universities – Bir and VandeVord are conducting an integrative investigation of "primary" blast injuries, or damages caused by the short duration, high amplitude pressure waves emitted from explosives. These injuries are now believed to be the reason behind the unprecedented number of soldiers that are returning from war with symptoms of mild to moderate traumatic brain injuries, many of whom don't recall being hit in the head.

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> **— Dr. Cynthia Bir**

"There's been a lot of research trying to determine if primary blast neurotrauma is actually a phenomenon, because for a while it was felt that you needed to have other aspects of a blast as well," said Dr. Bir, associate professor of biomedical engineering in the College of Engineering at WSU and lead investigator of the project. "But now we've realized that neurotrauma does occur from primary blast waves and that we need to investigate this. With such a strong history of neurotrauma research here at Wayne, it was an obvious choice to start looking at this."

A new kind of brain trauma

Until recently, soldiers were considered to have blast injuries if they had some sort of tangible mark, such as cuts from shrapnel or burns from the fireball. For brain trauma, hemorrhages and edema were long established indicators of injury. Yet, there is a large portion of soldiers returning from war without any of the traditional indicators of brain trauma who still suffer memory lapses, speech problems, difficulties with decision making, and other telltale signs of TBI.

"The soldiers that are really close to the explosion will get blown down and probably fall and hit their head," said VandeVord, assistant professor of biomedical engineering in

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the College of Engineering. "But the ones that are coming back with the mild TBI, they say that they didn't fall. They may have felt as if something weird was going on, but they're not falling and hitting their head."

Though it's difficult to estimate the number of TBI cases that have gone undiagnosed, the Defense and Veterans Brain Injury Center estimated in 2008 that 10 to 20 percent of all soldiers on duty in Iraq and Afghanistan have suffered some form of TBI. A TBI study released by the RAND Corporation in April 2008 fell in at the higher end of that percentage, estimating 19 percent or 320,000 soldiers experienced traumatic brain injury while deployed.

The startling prevalence of this form of mild TBI, coupled with the lack of understanding of how it works, is what prompted Bir and VandeVord to procure the blast tube. The twenty-foot long blast tube can be manipulated to simulate the pressure wave of an explosive without the additional elements of heat or shrapnel – allowing Bir and VandeVord to assess the effects of the pressure wave alone.

One of the main objectives for the blast tube is assessing how pressure waves cause brain damage – the types of cells that are damaged, how they become damaged, and the pathways by which the blast energy transfers through the brain. Equally important is establishing the threshold, either of pressure intensity or number of repeated exposures required for damage to occur.

Dr. Cynthia Bir, associate professor of biomedical engineering

The ultimate goal, Bir said, is to be able to recognize a soldier that has undergone mild traumatic brain injury through yet-to-be discovered biomarkers and provide treatments. "I think the thing this research is going to promote, especially within the Department of Defense, is the use of prophylactic medicine; giving soldiers some sort of medication either prior to going out in the field or directly after being exposed to prevent this injury from occurring," she said.

Before treatment or preventative medicine can be developed for mild TBI, however, researchers must first learn how to diagnose it. In addition to the blast tube, Drs. Bir and VandeVord are partnering with Dr. Mark Haacke, professor of radiology in the School of Medicine at Wayne State, to utilize a number of MRI methods that may provide information on how to recognize a brain with mild TBI. Using arterial spin labeling, or ASL, for instance, Bir and VandeVord are measuring blood flow rates in the brain before and after mild TBI has occurred. Susceptibility-weighted imaging, another type of MRI, detects micro-hemorrhaging. Lastly, using Magnetic Resonance Spectroscopy, they can assess possible changes in the levels of different kinds of metabolites and neurotransmitters due to blast waves.

The first cells hit

It is not certain which of these aspects of the brain will provide the best indicator that mild TBI has occurred, VandeVord said, but there have been hints that the initial change caused by pressure waves is a biochemical one. Funded by a $300,000 grant from the Department of Veterans Affairs, VandeVord exposed individual brain cells to pressure waves, to see which ones are

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affected by overpressure. She subjected neurons to immense pressures, but saw little negative effect. "We've gone to very high pressures, and neurons are surviving, which was strange to us," she said. She then turned her attention to glial cells, supporting cells of the brain that provide many different functions, including balancing nutrients, fighting infection and maintaining neurons' local environment. Over-active glial cells have been linked to neural damage in several neurodegenerative diseases, including Parkinson's disease. VandeVord ran the trial again, and found that unlike neurons, glial cells become activated in response to pressure waves, secreting molecules that can be toxic to neurons at high concentrations.

VandeVord's next step in research will be funded by a four-year, $600,000 TBI Intramural Investigator Award from the Congressionally Directed Medical Research Programs of the Department of Defense. With this award, she hopes to determine whether or not the toxic secretions are causing neuron apoptosis – or programmed cell death. "With these research efforts, if the neurons do die after being exposed to overpressure, we may begin to understand why," she said.

Dr. Pamela VandeVord, assistant professor of biomedical engineering

Regardless of whether glial cells turn out to be the turning point in understanding blast injuries, VandeVord is confident that Wayne State will be at the forefront of new developments in blast injury research in both imaging and blast simulation. "We believe that we are going to make a big difference," VandeVord said. "Other researchers in the field of blast injury seemed to be really impressed with how we are going about our research. We have spent a lot of time understanding blast physics, which is extremely important when entering this field. We made a point to train ourselves well in order to establish our group as leaders."

About Dr. Cynthia Bir:: Dr. Bir received a B.S. in nursing from Nazareth College, an M.S. in bioengineering from the University of Michigan, an M.S. in mechanical engineering and a Ph.D. in biomedical engineering from Wayne State University. Dr. Bir serves as the lead scientist on the Emmy award winning show, *Sports Science*, on the Fox Sports Network. She joined Wayne State University in 2000.

About Dr. Pamela VandeVord: Dr. VandeVord received a B.S. in physiology from Michigan State University, an M.S. in basic medical sciences and a Ph.D. in biomedical engineering from Wayne State University. She is an active member of the Society for Biomaterials, Biomedical Engineering Society, and Society of Women Engineers. She joined Wayne State University in 2002.