Treatment Strategies

Functional and Structural Changes in Cerebral Vasculature Following Exposure to Blast

Traumatic brain injury (TBI) is a leading contributor to combat related injury and death. Casualties from Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) have drawn increased attention to this injury. The subset of TBI cases due to blast injury present a particularly prominent and difficult problem. Explosion or blast is the most common cause of war injuries in OEF/OIF and the proliferation of improvised explosive devices (IEDs) has dramatically increased the numbers of blast overpressure (BOP)-induced TBI observed on the battlefield. Moreover, exposure to multiple low intensity blast events with or without overt concussion has an additive effect with long-term neurologic and other health consequences. A prominent neurological complication associated with severe blast-induced TBI in casualties from OIF and OEF was significant cerebral vasospasm. Despite clinical indications of vascular insult and supporting experimental data in animals, there remains a paucity of information on specific structural and functional changes in the cerebral vascular space that occur after blast exposure. To further understand this complication, researchers at the Naval Medical Research Center (NMRC) are evaluating alterations within the cerebral vasculature in a rat model of blast-induced TBI. The studies being conducted use an established rodent model to assess the effects of a single exposure to varying BOP intensities on cerebral macro- and micro-vasculature up to six months after exposure with an emphasis on identifying physiological underpinnings associated with cerebral vasospasm. Study techniques include functional indices of vascular function using intravital microscopy to assess changes within the cerebrovascular responsiveness after exposure to BOP. Structural assessment is being accomplished using electron microscopy coupled with immunostaining techniques to visualize changes to vascular endothelium, including the glycocalyx, assessment of tight junctions, perivascular edema, and changes in endothelin-1 within the vasculature. Initial results show that blast-exposed rats demonstrate cerebrovascular weakening, reduction of the endothelial glycocalyx structure in cerebral vessels, and blunting of induced vasoconstriction in cerebral arteries. Results also suggest that functional changes in cerebrovascular responses after blast occur in a time-dependent manner. Additional studies will be conducted to assess the effects of single and multiple exposures to varying BOP intensities on cerebral macro- and micro-vasculature up to six months after exposure. Characterization of cerebrovascular reactivity after blast-induced TBI is critical to our understanding of vascular pathology in blast-exposed military personnel. It is important for developing potential treatment strategies for neurological symptoms in Service Members exposed to blast.