Preclinical Models of Blast Injury

Correlation of Blast Overpressure Exposure with Brain Injury Severity, Cellular Pathology, and Types of Tissue Injury across Different Brain Regions

Blast exposure and related injuries are a significant threat to the health of Service members in training environments and in combat, and by extension, a threat to overall Force readiness. In particular, traumatic brain injuries (TBI's) from blast exposure are a signature injury of the post 9/11 conflicts (*Elder and Cristian 2009, Hoge et al. 2008, Moore and Jaffee 2010*). Although there exists a large body of work examining blast exposures and blunt impact on brain injury, correlations to the human condition are less well defined. In work performed at New Jersey Institute of Technology, the researchers focused on developing validated master dose response curves for blast exposure which correlate the biomechanical properties of blast waves to specific types of injury on brain tissue in a manner that is independent of blunt injury. The long-term objective of the work is to be able to produce an interspecies transfer function and develop a human Blast Injury Criterion which can be used to assess the risk of brain injury in humans exposed to blast. The work seeks to build upon and unify past efforts in blast-related brain injury by comprehensively assessing blast injury in a single, specific, and validated shock tube.

Notable findings from the last year highlight differences in pathological response of the brain iin rats between blunt and blast brain injury (Figure 1; *Arvind et al. 2017*). In work presented at the 2017 National Neurotrauma Society Meeting the researchers reported upregulation of the superoxide producing enzyme, nicotinamide adenine dinucleotide phosphate nicotinamide adenine dinucleotide phosphate oxidase 1 (NOX1), in a number of brain regions in response to blast exposure (*Chandra et al. 2017*). This response is not observed following blunt brain injury, suggestive of different oxidative stress responses for different mechanisms of brain injury. In addition, neurodegenerative markers were not observed in response to blast exposure. Primary blast exposure caused damage resulting in disruption of the blood-brain barrier at blast overpressure levels associated with all severities of brain injury. Furthermore, the extent of tissue injury resulting from blast exposure varied throughout the brain and was determined by relative density in neurons, astrocytes, and vascular tissue.

Development of dose-response curves correlating blast exposure levels to specific types of pathological findings will inform the development of personal protective equipment for Service members and aid in developing injury prevention standards.

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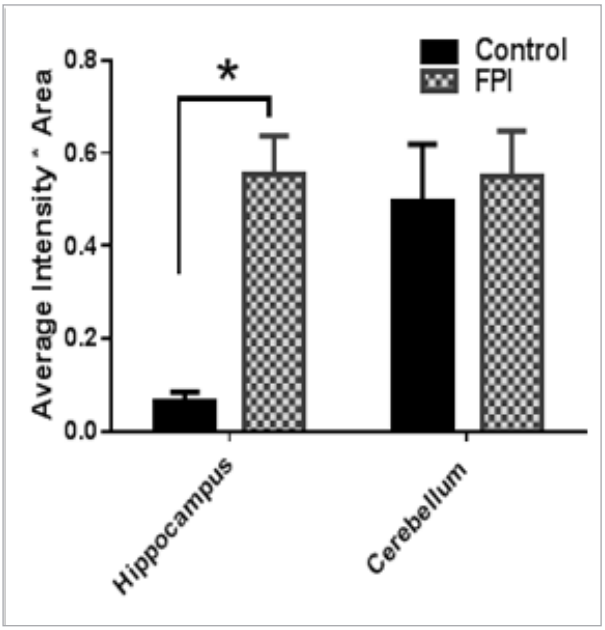

FIGURE 1: Immunofluorescence quantification of NOX1 in blunt induced trauma (FPI) displays a different mode of change in hippocampus and cerebellum. A limited study performed to make a comparative account of injury outcome between blast and blunt TBI shows that NOX1 increased in ipsilateral side of hippocampus (contralateral side did not show changes) but not in cerebellum where the injury was induced in the right parietal cortex. These data strongly suggest that the pattern of injury between blast and blunt models of trauma differ with regard to pathophysiological outcomes. Quantification of florescence intensities of NOX1 in hippocampus and cerebellum. *, p<0.01-0.05. (Figure used with permission from the authors)

REFERENCES:

Arvind, A., Kakulavarapu, R., Long, M., Chandra, N., and Pfister, B. 2017. "Characterization of a Combined Model of Blast and Blunt Injury." J Neurotrauma 34 (13):A90-A91.

Chandra, N., RamaRao, K., Iring, S., Younger, D., Aravind, A., Pfister, B., and Skotak, M. 2017. "Blast-Induced Traumatic Brain Injury Displays a Unique Pattern of Spatial Neuropathology." J Neurotrauma 34 (13):A88-A89.

Elder, G. A., and Cristian, A. 2009. "Blast-Related Mild Traumatic Brain Injury: Mechanisms of Injury and Impact on Clinical Care." Mt Sinai J Med 76 (2):111-8. doi: 10.1002/msj.20098.

Hoge, C. W., McGurk, D., Thomas, J. L., Cox, A. L., Engel, C. C., and Castro, C. A. 2008. "Mild Traumatic Brain Injury in U.S. Soldiers Returning from Iraq." N Engl J Med 358 (5):453-63. doi: 10.1056/NEJMoa072972.

Moore, D. F., and Jaffee, M. S. 2010. "Military Traumatic Brain Injury and Blast." NeuroRehabilitation 26 (3):179-81. doi: 10.3233/NRE-2010-0553.