Injury Models

Sensitive Indicators and Risk Factors of Blast-Induced Neurodegeneration in Hippocampus

The pressure profile generated from shock tube devices does not match the profile produced by explosives (Chen and Constantini, 2013). To specifically study the effects of realistic blasts, a novel procedure was recently developed by researchers at ARL that generates reproducible shockwaves from a detonated explosive (Zander et al., 2015). The procedure uses a highly controlled construct of research department explosives (RDX), the major component of C-4 explosive and one of the most powerful military explosives. In order to examine the direct effects of explosives on brain tissue, the present study utilized in vitro slice cultures of the rat hippocampus. The hippocampus is the main focus of this study not only due to it being distinctly vulnerable to traumatic and excitotoxic injuries, but also because it is a region that is important for higher order brain functions, which expresses synaptic plasticity to compute diverse information and is involved in routing the encoded spatial, emotional, and reward information to other brain areas. Cultured hippocampal slices were placed in a specialized blast chamber in which defined assemblies of RDX were detonated outside the chamber to produce realistic and reproducible blast shockwaves. This is the first study using the in vitro blast paradigm to apply RDX detonations to intact brain tissue, and showed that multiple explosive blasts alter the levels of important synaptic markers: down-regulation of synaptophysin, synaptotagmin, and synapsin 2b and up-regulation of synapsin 2a. Thus, shockwaves from detonated RDX explosive appear to produce a unique type of pathology comprised of distinct reductions in synaptic proteins before cellular deterioration sets in. Identification of molecular indicators of blast-induced injury to neurons in sensitive brain areas could drive new therapeutic opportunities for mitigating the impacts of blasts to Service Members, independent of materiel solutions.