Preclinical Studies for the Treatment of Blast-related Injuries

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 the Army Research Laboratory (Adelphi, Maryland) that generates reproducible shockwaves from a detonated explosive (*Zander et al. 2015*). The procedure uses a highly controlled construct of research department eXplosives (RDX). A major component of C-4 explosive, RDX is one of the most powerful military explosives. 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 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, 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, synapsin 2b, and up-regulation of synapsin 2a. Surprisingly, very little cell death occurred as a result of multiple exposures to RDX. Thus, shockwaves from detonated RDX explosive appear to produce a unique type of pathology comprised of distinct reductions in synaptic proteins in the absence of neuronal deterioration. The resulting molecular 'injury' could alter synaptic communication leading to deficits experienced by Service members exposed to mild injury from blast.

REFERENCES:

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