# Oxidative Stress and Antioxident Treatment

## Characterization of Blast Injury in an Animal Model to Support Development of a Human Blast Injury Criterion

There is a large body of work examining blast exposures and blunt impact on brain injury in animal models, but their correlations to the human condition are less well defined. Researchers at the New Jersey Institute of Technology (NJIT; Newark, NJ) are working toward a validated master dose-response curve for blast exposure that correlates the biomechanical properties of blast waves to specific brain tissue injuries in a manner that is independent of blunt injury. This goal furthers their long-term objective to produce an interspecies transfer function and develop a human "Blast Injury Criterion" for assessing the risk of brain injury in humans exposed to a single or repeated blast.

A number of findings towards this aim have recently been published. In rats exposed to a single 180 kPa overpressure event in a shock tube, levels of NOX 1 and NOX 2 (nicotinamide adenine dinucleotide phosphate oxidase 1 and 2), a superoxide producing enzyme, in the cerebellum and cerebral hemisphere were significantly higher than in sham controls four hours after exposure (*Rama Rao et al., 2018*). Correspondingly, levels of superoxide were significantly higher in the frontal cortex, hippocampus, thalamus, and cerebellum of blast-exposed animals than in sham controls. These observations indicate that there is an increase in oxidative stress and oxidative damage occurring in the brain in the acute phase of blast exposure.

In a separate study of a single blast event, rats exposed to 180 kPa overpressure experienced disruption of the blood-brain barrier as measured by the concentration of tracer agents (e.g., Evans blue dye and sodium fluorescein) peaking in the brain parenchyma four hours after injury and returning to pre-injury levels within 24 hours (*Kuriakose, et al., 2018*). The most robust changes occurred in the frontal cortex, striatum, and thalamus, while minimal to no statistically significant extravasation was observed in the cerebellum, demonstrating an anterior to posterior pattern of differential blood-brain barrier permeability. In addition, separate studies on rats exposed to a single 110-130 kPa overpressure event suggest that the highest intensity of electrophysiological activity occurred in cerebellum within the first 24 hours after injury (*Ordek et al., 2018*).

Ultimately, this work supports the development of dose-response curves correlating blast exposure levels to specific types of pathological findings. This knowledge will inform the design of improved diagnostics and personal protective equipment for Service members.

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## REFERENCES:

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