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14. ABSTRACT The etiology of blast-induced traumatic brain injury (TBI) is largely undefined. Along with reducing mortality, in preliminary experiments Kevlar vests significantly protected against BOP-induced neuropathological changes in rats. We postulate that: 1) much of the blast-induced fiber degeneration in brain results from pressure surges transmitted through the vasculature that elicit a series of intracranial disruptions, and 2) Kevlar vests are neuroprotective by uncoupling this pressure transmission following exposure to blast. Using a compression driven shock tube, we compare external, systemic (e.g. vascular arterial and venous), and central (e.g. intracranial pressure) BOP-induced pressure changes, and assess the impact of Kevlar vests on these changes. We seek to: 1) determine if measured pressure changes are blast severity-dependent and correspond with outcome measures, and 2) assess the impact of Kevlar vests on measured BOP-induced pressure changes and outcome measures and establish whether a protective vest encasing the thorax ameliorates blast-induced brain injury, pointing to a significant contribution of the effects of blast on the thorax to brain injury. These studies will provide critical insights into the etiology of blast-induced brain injury, and will advance the development of mitigation strategies.					
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INTRODUCTION:

Body armor has made blast injuries survivable; consequently, we speculate that to a large extent blast-induced head injuries have emerged among troops who without body armor would have simply been killed in action as a result of injury to more vulnerable organs such as the lung. Serendipitously, in a preliminary experiment we noted that along with reducing mortality, lung injury, and cardiovascular disruptions by blast overpressure (BOP), Kevlar vests protected against BOP-induced neuropathological changes in rats. These preliminary findings suggested that a protective vest encasing the thorax might ameliorate blast-induced brain injury, pointing to a significant contribution of the effects of blast on the thorax to brain injury pathophysiology. We hypothesize that much of the blast-induced fiber degeneration in brain results from pressure surges transmitted through the vasculature (venous as well as arterial) that elicit a series of intracranial disruptions, and that Kevlar vests are neuroprotective by uncoupling this pressure transmission following exposure to blast.

BODY:

To address how BOP effects on the thorax contribute to brain injury and to evaluate how Kevlar vests protect the brain, we propose to measure, compare, and correlate external, systemic (e.g. vascular arterial and venous), and central (e.g. intracranial pressure) BOP-induced pressure changes, and assess the impact of Kevlar vests on these changes. In particular, we will, use a compression driven shock tube to: 1) determine if measured pressure changes are blast severity-dependent and correspond with neuropathological and neurobehavioral outcome measures, and 2) assess the impact of Kevlar vests on measured BOP-induced pressure changes and outcome measures. As detailed below, in addition to neuropathological and neurobehavioral evaluations, these outcome measures will include assessments of blood-brain barrier integrity and cerebral blood flow measurements, since we postulate that the cerebrovasculature plays a pivotal role in blast-induced brain injury pathophysiology, and is likely to be disrupted by blast-induced perturbations.

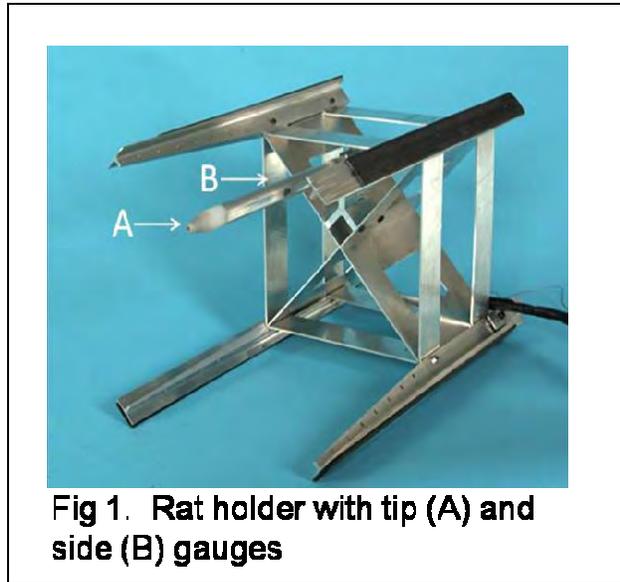
KEY RESEARCH ACCOMPLISHMENTS:

During this reporting period, we:

- Developed and utilized a new rat holder that records the static and dynamic pressures that each rat is exposed to in a non-rigid restraint device that neither shields the experimental subject nor contributes to the injury. This is a fundamental and necessary improvement over the previous holder.
- Using piezoresistive gauges to record both side-on and head-on pressures, mapped the blast simulation conditions along the longitudinal axis of the shock tube and established the optimal tube position to subject rats to BOP exposures.
- Simultaneously recorded intracranial and extracranial (i.e. external to the rat) pressures resulting from airblasts of varied intensities and compared the intracranial pressure responses recorded in rats wearing and not wearing

protective vests. Intracranial pressure responses measured to date do not appear to be altered by the protective vest.

During the reporting period, we recognized several significant technical impediments for our proposed research stemming from our rat holder and its restricted position at the mouth of the shock tube. Correction of these impediments was an essential



prerequisite for progress on the defined milestones and collection of valid data. Blast generates an air shock front imparting effectively instantaneous increases in static and dynamic pressure conditions. The distinction regarding the incident blast flow conditions (i.e. static and dynamic pressures) and target loading have important implications with regard to the mechanisms for blast injury and cellular stresses as well as the proper experimental simulation of blast. In particular, the positioning of the experimental subject within the shock tube greatly influences exposure conditions and determines the relative

contributions of side-on and dynamic pressures to the injury. After gaining a better appreciation of blast physics, we recognized that it is critical to be able to vary the position of rats within the shock tube using a holder that is minimally intrusive regarding rat exposure to shock wave and associated air movement. Our original rat holder, which fixed the rat at a set position at the mouth of the tube without gauges to record the specific pressure conditions at this position, was inadequate in this regard. We therefore designed a new rat holder that we now utilize that enables us to record the static and dynamic pressures that each rat is exposed to in a non-rigid restraint device that neither shields the experimental subject nor contributes to the injury (fig 1). The new holder can be positioned anywhere throughout the length of the shock tube and also better accommodates the instrumentation required for physiological recordings. As noted previously, although this unforeseen requirement has slowed our data collection from our original time projections, we are confident that we can complete the study within the overall time schedule with vastly improved, artefact-free data.

Recognizing that blast simulation conditions vary along the longitudinal axis of the shock tube, we have mapped these positional differences using comparative tip and side gauge recordings. As seen in table 1, greatest differences in pressure impulses become evident as one approaches the mouth of the shock tube, and are much more pronounced immediately outside the tube. In particular, the impulse ratio changed dramatically immediately outside the mouth of the tube, where total pressure impulse increased by factors of 100-fold reflecting an even more pronounced potential biomechanical influence of dynamic pressure (i.e. blast wind) in the exit-jet flow. This is a general concern with all exposures outside of a tube (such as occurred with our previous holder). The design of the new holder facilitates our control and quantitation of

the individual components of blast contributing to injury. Through manipulation of controllable shock tube experimental parameters (e.g. driver volume, tube position, Mylar membrane thickness, and type of gas), one can recreate a wide variety of conditions experienced in different blast scenarios, and also comparatively establish which of these parameters (e.g. peak pressure vs. impulse) has the greatest influence on physiological perturbations and injury mechanisms.

The shock tube consists of a 2.5 ft long by 1 ft diameter compression chamber and a 15 ft long by 1 ft diameter expansion chamber separated by a Mylar membrane. Air pressures within the tube and intracranial pressures within the rat skull were recorded with anesthetized rats positioned in a transverse prone position 2.5 ft from the mouth of the tube. Rats were tested with and without Kevlar vests. Pressures were recorded using 127 micron thick membranes and 254 micron thick membranes which typically produce side-on peak pressures of 12 and 20 psi, respectively. Figure 1 shows pressure waveforms generated using a 127 micron thick mylar membrane and recorded by the pressure sensors inside the tube (side-on and tip piezoresistive gauges) and inside the rat brain (Millar transducers). Each waveform consists of a positive overpressure wave followed by a negative underpressure wave and return to ambient pressure. In this figure, the total (tip) pressure approached 13 psi while the static (side) and intracranial pressure approached 10 psi. The overpressure durations of intracranial and static pressure were quite similar, while the total overpressure measured by the tip gauge had a longer duration. Overall, the induced overpressure profile recorded intracranially and statically in the air surrounding the rat do not vary much in terms of magnitude, impulse, and duration, corroborating the findings of Chavko et al. (2007). The total pressure, which is a combination of static and dynamic pressure, had a higher peak pressure and lasted longer than the static and intracranial pressure.

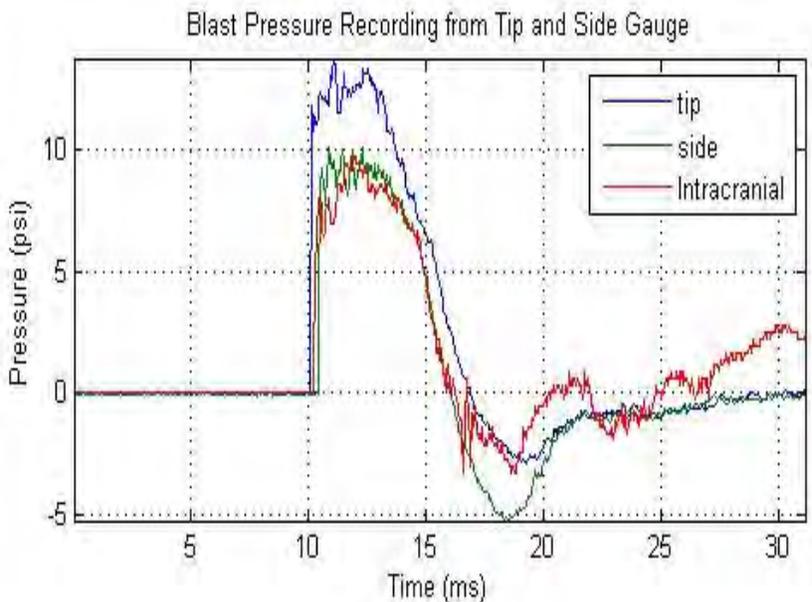


Figure 1. Tip, side and intracranial pressures recorded during the blast.

With the unanticipated time required to initially develop a gauged shock tube rat holder and characterize blast conditions within the tube, completion of this milestone is estimated to be delayed by 6-8 months.

Accomplishment: Peak pressure, impulse, and duration did not differ between protective vest and no protective vest test groups (table 2), indicating that immediate ICP responses to BOP are minimally affected by protective vests. In ongoing experiments, vascular pressure responses to BOP are now being collected to establish whether they are blast severity dependent and affected by protective vests.

Table 2. BOP parameters with and without vests

127 micron thick membrane	Vest	No Vest
Peak Total pressure (psi)	15.20	13.72
Peak Static Pressure (psi)	10.19	10.10
Peak Intracranial Pressure (psi)	8.22	9.63
Total Overpressure Impulse (psi-ms)	62.33	59.85
Static Overpressure Impulse (psi-ms)	38.39	40.13
Intracranial Overpressure Impulse (psi-ms)	32.64	38.96
Total Overpressure Width (ms)	6.85	6.80
Static Overpressure Width (ms)	5.58	5.60
Intracranial Overpressure Width (ms)	6.55	6.00
254 micron thick membrane	Vest	No Vest
Peak Total pressure (psi)	24.28	22.76
Peak Static Pressure (psi)	14.96	15.68
Peak Intracranial Pressure (psi)	16.65	14.31
Total Overpressure Impulse (psi-ms)	110.58	107.80
Static Overpressure Impulse (psi-ms)	59.02	65.07
Intracranial Overpressure Impulse (psi-ms)	60.82	61.29
Total Overpressure Width (ms)	9.28	8.95
Static Overpressure Width (ms)	6.48	10.10
Intracranial Overpressure Width (ms)	6.93	8.45

REPORTABLE OUTCOMES:

Manuscripts

Long, J. B., Tong, L., Bauman, R. A, Atkins, J. A, Januszkiewicz, A. J., Riccio, C., Gharavi, R., Shoge, R., Parks, S., Ritzel, D. V., and Bentley, T. B. Blast- induced traumatic brain injury: using a shock tube to recreate a battlefield injury in the laboratory. IFBME Proceedings 30. 2010.

Abstracts/Presentations

Gharavi R.B., Shoge R.O., Long J.B., and Bentley T.B. Characterization of an air-driven shock tube used to recreate battlefield traumatic brain injuries. National Neurotrauma Symposium, June 2010.

Riccio C, Bentley T.B., and Long J.B. Blast overpressure injury in rats produces widespread fiber degeneration. National Neurotrauma Symposium, June 2010.

CONCLUSION:

Following the necessary design and development of a gauged rat holder that records the static and dynamic pressures specifically occurring in the immediate environment of the rat with each airblast, blast exposure conditions were mapped throughout the length of the shock tube. A position 2.5 ft from the mouth of the tube was determined to be optimal for BOP exposures using a non-rigid restraint device that neither shields the experimental subject nor contributes to the injury. Using this holder, simultaneously recorded intracranial and extracranial (i.e. external to the rat) pressures resulting from airblasts of varied intensities were recorded and compared in rats wearing and not wearing protective vests. The intracranial pressure responses measured to date are nearly identical to the external static pressures and do not appear to be altered by the protective vest.

REFERENCES:

Chavko M, Koller WA, Prusaczyk WK, McCarron RM. Measurement of blast wave by a miniature fiber optic pressure transducer in the rat brain. J Neurosci Methods . 2007 Jan 30;159(2):277-81.

APPENDICES: NONE