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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.

15. SUBJECT TERMS
Traumatic Brain Injury (TBI), Kevlar Vests, Neuroprotection

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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 em erged 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 disrupt ions by blast overpressure (BOP), Kevlar vests protected against BOP-induced neur opathological 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 c ontribute to brain injury and to evaluate how Kevlar vests protect the brain, we pr opose to measure, compare, and correlate external, systemic (e.g. vascular arterial and venous), and central (e.g. intracranial pressure) BOP-induced pressures changes, and assess the impact of Kevlar vests on these changes. In particular, we will, us e a compression driven shock tube to: 1) determine if measured pressure changes are blast severity-dependent and correspond with neuropathological and neurobehav ioral outcome measures, and 2) assess the impact of Kevlar vests on measured BOP- induced pressure changes and outcome measures. As detailed below, in additi on to neuropathological and neurobehavioral evaluations, these outcome measures will in clude assessments of blood-brain barrier integrity and cerebral blood flow measurem ents, 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:

- Simultaneously recorded the pressures within the shock tube resulting from airblasts of varied intens ities (generated with rupturabl e membranes of different thicknesses) and the corresponding intrac ranial and intravascular pressure responses within the rat (specific aims 1 & 2). With increased Mylar membrane thicknesses, greater blast pressure s were generated and yielded correspondingly greater intracranial and intravascular pre ssures in the rats positioned 2.5 ft within the mouth of the tube. Acro ss all blast pressure exposure conditions, intracranial pressures closely corresponded to external side-on pressure recordings, revealing that the skull provides littl e protection against elevated pressures in rats (Fig 1 and

Table 1). With increased membrane thi cknesses, peak pressures and pressure impulses both increased for side-on and ti p gauge recordings in the tube, and yielded correspondingly elevated and prolonge d intracranial and intravascular pressure responses.

- Compared pressure recordings at the m outh of the tube and withi n the tube. Since beginning this project we lear ned that positioning the within the tube is preferred for optimal simulation of blast flow condi tions, and most recordings have been made with subjects at this position using an instrumented rat holder (Fig 2). Nevertheless, since the protective effect of vests upon whic h this proposal is based were originally observed at the mouth of t he shock tube, we also made pressure recordings and evaluated rats exposed to blast at this pos ition as well. Flow conditions (i.e. pressures) were very different at the mouth of the tube (Fig 3). Although for a given membrane thickness the intracranial and intr avascular pressures recorded in rats at the mouth of the tube differed substantially from those s een in rats positioned 2.5 ft within the tube, they closely resembled t he external pressures measured at these positions and also were not substantially altered by protective vests (Fig 10, specific aims 1 & 3).

- Compared the intracranial pressure re sponses recorded in rats wearing and not wearing protective vests at different blas t overpressure intensities at different positions within the shock tube (mouth of tube and 2.5 ft within the tube). Intracranial pressure responses measur ed to date do not appear to be altered by the protective vest at either tube position (Fig 4 & Fig 10, specific aim 3).

- Determined that in addition to causing large pressure responses in rats, airblast in the shock tube also caused large accelerati ons, which could contribute to the brain injuries resulting from these exposure c onditions. Speculating that the salutary effects of protective vests might resu lt from diminished acceleration and displacement, these parameters are being examined in vested and unvested experimental subjects (Fig 9).

- Evaluated the effects of protective vests on blast-induced blood-brain barrier breakdown by measuring Evans blue dye extravasation into the brain parenchyma at different time intervals after airblast exposure (specific ai m 4). Experiments are ongoing and reveal significant measurable blood-brain barrier disruptions. To date, Evans blue dye extravasation has not been signi ficantly diminished in rats exposed to airblast wearing protective vests at either 2 or 5 hours post-blast.

- Recorded blast severity-dependent neurobehav ioral disruptions using the Morris water maze and ambulation on a rotating pole (Figs 5-7, specific aim 2). With experimental modifications that yielded a higher fidelity simulation of blast (e.g. new holder positioned 2.5 ft withi n the shock tube), neurobehavioral disruptions and associated histopathological changes were greatly reduced from what was

previously seen with rats exposed at the mouth of the tube (which were less tightly secured in a rigid holder, and at this position experienced greater turbulence and dynamic flow conditions). Nevertheless, we have established that, when positioned 2.5 ft within the shock tube, significant performance disruptions in both neurobehavioral tests can be seen at 21 psi peak overpressures. Although less pronounced than previously reported, these behavioral deficits are associated with neuropathological changes, characterized primarily by fiber degeneration that is particularly prominent in cerebellum, optic tract, and internal capsule (Fig 8).

REPORTABLE OUTCOMES:

Two manuscripts in preparation.

Abstracts/Presentations

Shoge, R.O. Pressure profiles of shock tube exposures. Invited platform presentation at the Advanced Technology Applications for Combat Casualty Care (ATACCC) Meeting, St. Pete's Beach FL, Aug, 2010.

Riccio C., Bentley T.B., and Long J.B. Blast overpressure injury in rats produces widespread fiber degeneration. Poster at the Advanced Technology Applications for Combat Casualty Care (ATACCC) Meeting, St. Pete's Beach FL, Aug, 2010.

Long, J.B. Experimental Evaluation of Blast-induced Traumatic Brain Injury in Rats Using a Cylindrical Shock Tube. Invited speaker at the Third DOD Brain Injury Computational Modeling Expert Panel Meeting, Johns Hopkins University Applied Physics Laboratory, Laurel MD, Dec 2010.

Shoge, R.O. Experimental Evaluation of Blast-induced Traumatic Brain Injury in Rats Using a Cylindrical Shock Tube. Invited speaker at the National Capital Region TBI Research Symposium. April 5, 2011.

CONCLUSION: A high fidelity laboratory simulation of blast has been achieved using an air driven shock tube and a custom designed gauged rat holder that records the static and dynamic pressures specifically occurring in the immediate environment of the experimental subject for each airblast exposure. Intracranial and intravascular pressure recordings have been made and reveal that blast pressure responses in the rat closely resemble those recorded in the adjacent atmosphere with respect to both magnitude and timing. Protective vests have not altered these pressure responses, nor under these conditions have they substantially altered neurobehavioral disruptions resulting from blast exposures.

REFERENCES: None

APPENDICES: None

SUPPORTING DATA: All figures and/or tables shall include legends and be clearly marked with figure/table numbers.

Fig 1. ICP pressure closely resembles atmospheric pressure within the shock tube.

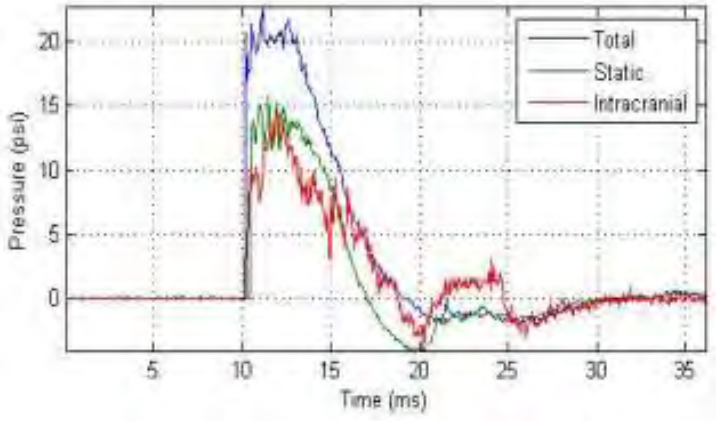


Fig 2. Instrumented rat holder records static and total pressure at the experimental subject.

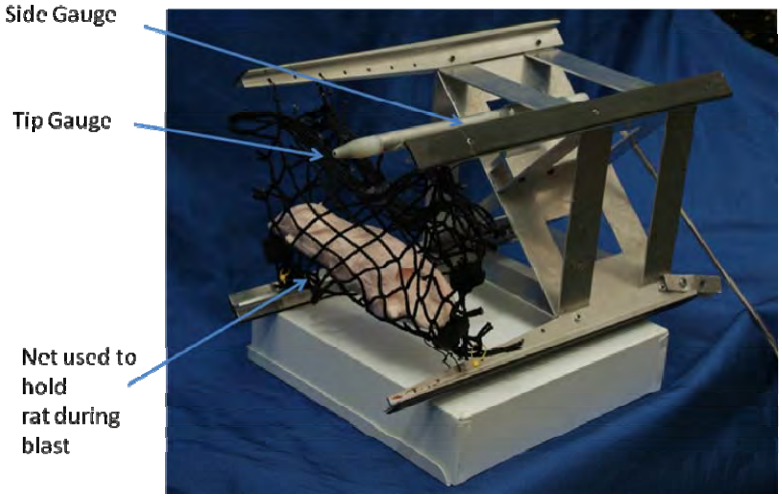


Fig 3. Flow conditions vary along the length of the shock tube, particularly at the mouth.

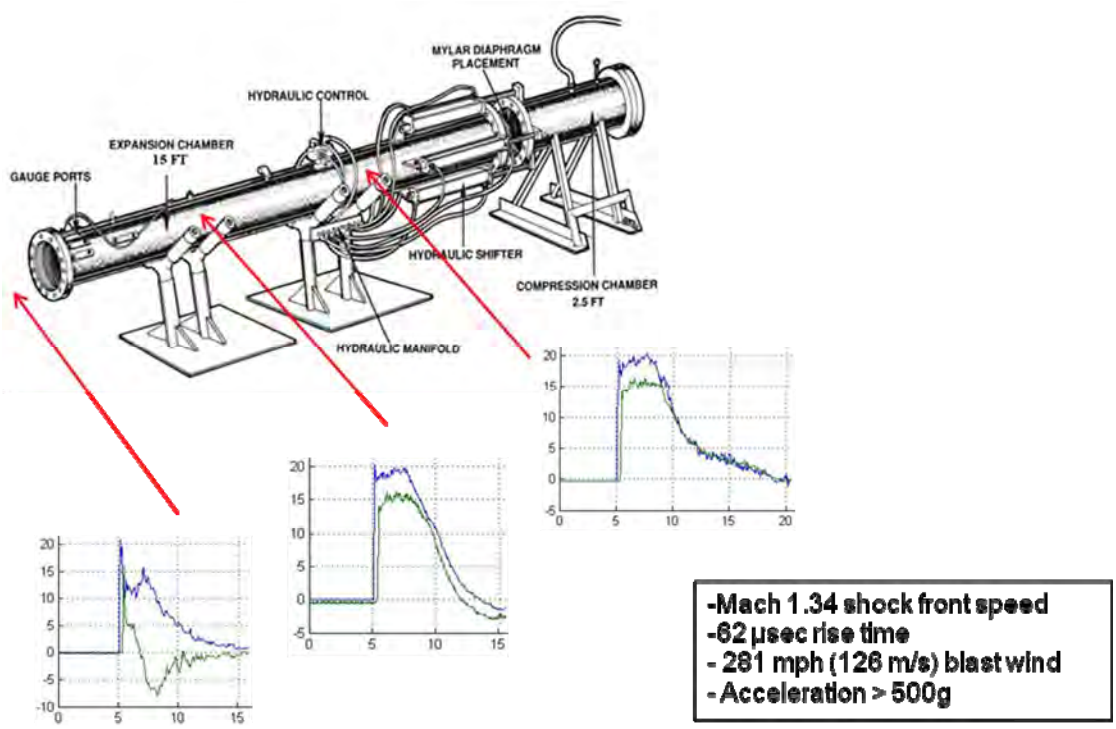


Fig. 4. Pressures measured in rats with and without protective vests (16 psi Static Pressure Blast)

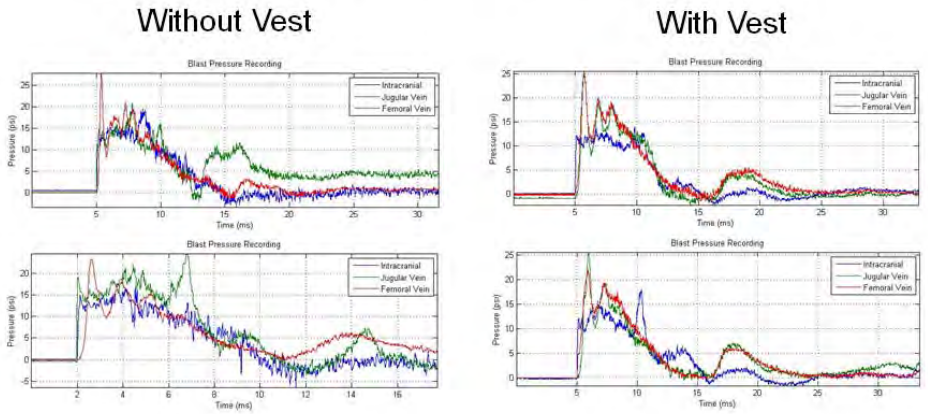


Fig. 5. Rotating pole test

Functional deficits (e.g. vestibulomotor disruption assessed while traversing a rotating pole)

Fig 6. Rotating pole performance after 16 psi blast exposures

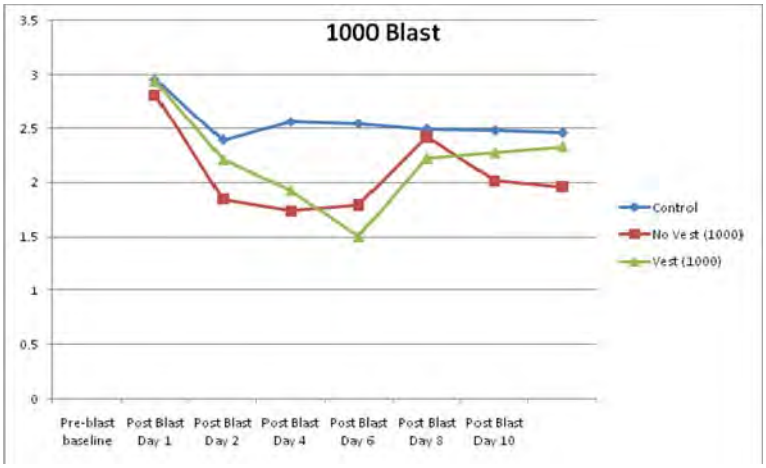


Fig 7. Morris water maze performance after 16 psi blast exposures

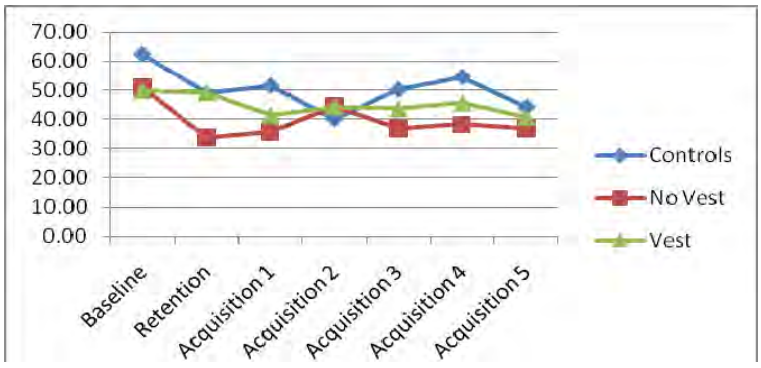


Fig 8. Blast-induced fiber degeneration

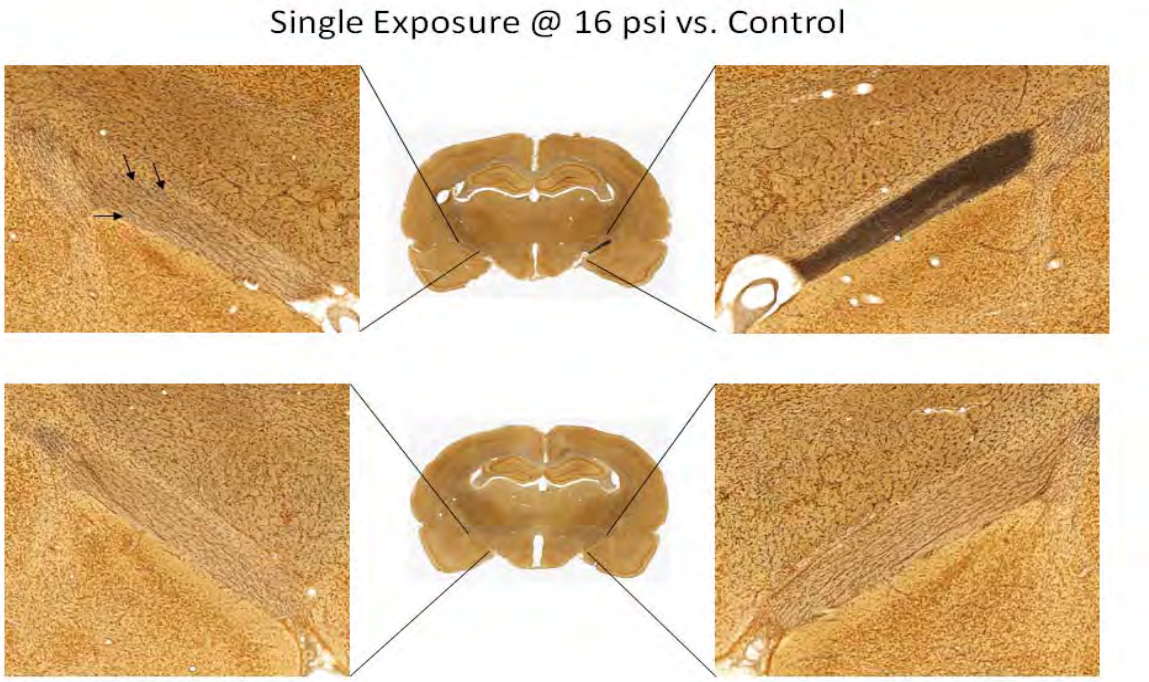


Table 1. Average (Standard Deviation) BOP Parameters Recorded With and Without Vest Inside the Tube
16 psi Static Pressure Blast

	Vest (N=4)	No Vest (N=4)
Outside Air Peak Total Pressure (psi)	21.5	
Outside Air Peak Static Pressure (psi)	16.3	
Peak Intracranial Pressure (psi)	17.38 (1.39)	18.43 (1.13)
Peak Intrajugular Vein Pressure (psi)	27.94 (5.74)	22.40 (1.37)
Peak Femoral Intravenous Pressure (psi)	19.26 (1.88)	22.57 (1.38)
Outside Air Total Pressure Impulse (psi-ms)	98.0	
Outside Air Static Pressure Impulse (psi-ms)	71.9	
Intracranial Pressure Impulse (psi-ms)	86.94 (6.45)	72.93 (1.01)
Intrajugular Vein Pressure Impulse (psi-ms)	89.39 (1.96)	84.36 (1.17)
Femoral Intravenous Pressure Impulse (psi-ms)	97.24 (4.18)	75.61 (1.05)
Outside Air Total Pressure Duration (ms)	8.4	
Outside Air Static Pressure Duration (ms)	6.7	
Intracranial Pressure Duration (ms)	9.02 (0.88)	6.96 (1.04)
Intrajugular Vein Pressure Duration (ms)	8.89 (0.37)	8.63 (1.29)
Femoral Intravenous Pressure Duration (ms)	9.33 (0.29)	8.02 (1.20)

•While peak intracranial and vascular pressures did not differ much between vest and non-vested animals, pressure durations and impulses measured inside the rat were smaller for animals wearing chest protection vs. not.

Fig 9. Head acceleration (g) measured inside the tube using current net holder design (16 psi Static Pressure Blast)

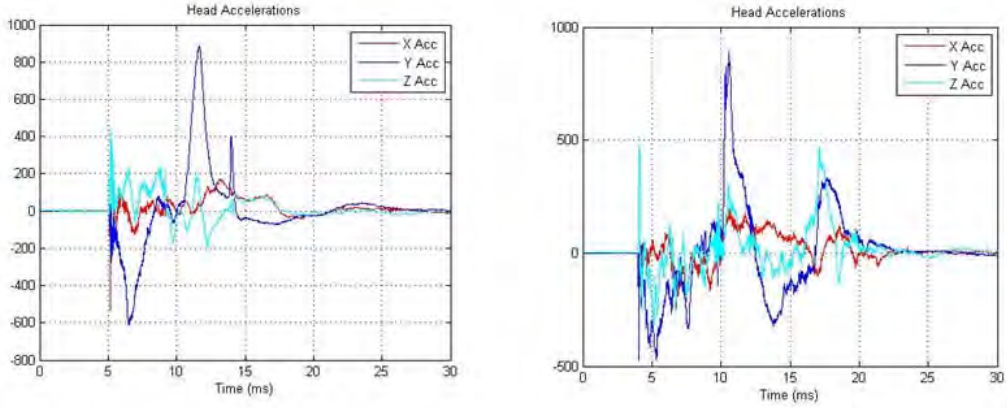
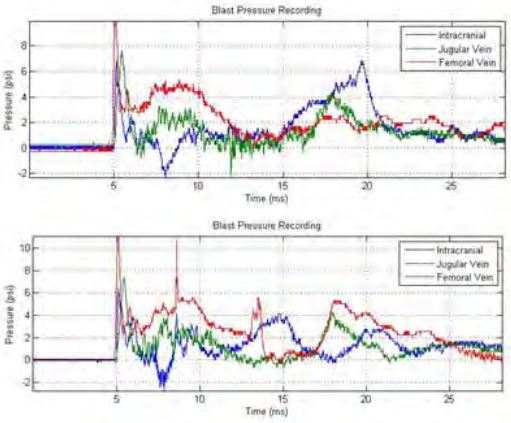


Fig 10. Pressures measured in rats with and without vests at the mouth of the tube (16 psi Static Pressure Blast)

- Without Vest



- With Vest