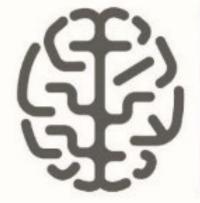
CBN



Center for Injury BioMechanics, **Materials and** Medicine



Our

Mission

Integrating engineering, biology and medicine to address **Traumatic Brain Injury (TBI)**

through experimental, computational and clinical methods.



"Our mission is to help soldiers and civilians by understanding why and how blast and blunt trauma causes injury to the brain. We built unique blast wave and blunt injury platforms using animal, PMHS and in-vitro models to address complex questions. Our holistic and collaborative approach explores Traumatic Brain Injury to save and improve lives." – Bryan J. Pfister, PhD (Director)

Innovative Approaches to Complex Problems

The CIBM3 employs a full spectrum of unique preclinical platforms for the study of blunt and blast injuries from cell culture to full-scale human models.

- Field validated shock generation facility with the ability to fine tune blast wave parameters.
- Precise biomechanical replication of injury to the brain using uniquely engineered platforms with a focus on mild and repetitive TBI.

Engineered Solutions for Traumatic Brain **Injury Research**

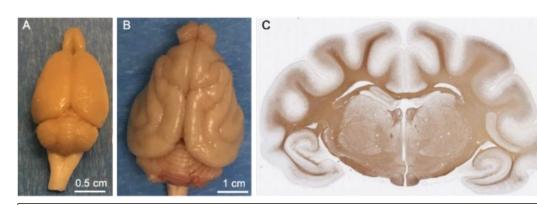
Key Capabilities

- Engineered platforms for blast and blunt injury
- *In vitro* and *in vivo* experience \bullet
- Large animal modeling
- Cadaveric testing experience ${}^{\bullet}$
- Functional testing / electrophysiology / EEG
- Animal behavior: motor, learning, memory, anxiety, \bullet sleep, conditioned responses
- Histological, biomolecular and imaging facilities

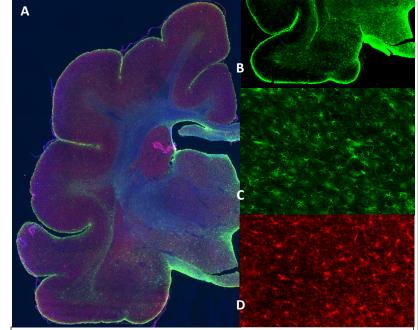


- Fully integrated human scale head-brain, physical model and computational model with validated experimental measurements.
- In-vitro neuronal stretch and blunt TBI animal modeling controlling injury rate and duration that are essential parameters to injury outcome.
- State of the art animal imaging and functional assessments with expertise in chronic inflammation, behavioral changes, electrophysiology and loss of neurons.
- Blast and blunt head injury platforms to experimentally assess and validate protection systems.

Ferret Model of TBI



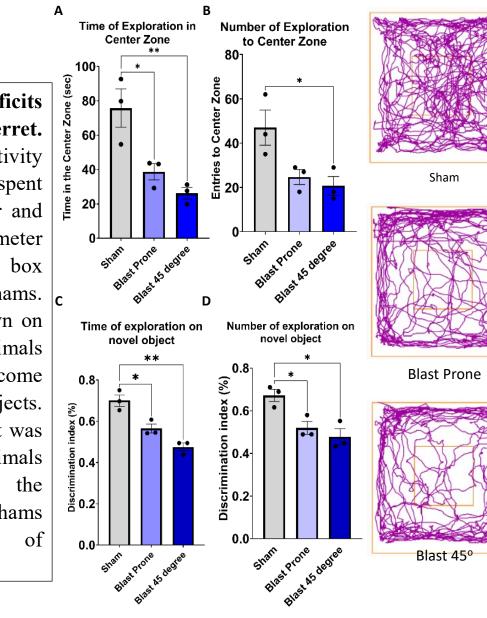
Rat vs. ferret brain structure. Compared to the adult rat (A), the ferret (B) has a gryrified brain with a more similar white matter content to the human brain. (C) A coronal section of the ferret brain labeled for myelin protein showing large amounts of white matter which allows for neuropathological focus on the cortical sulci and white:gray interfaces, which are particularly vulnerable to TBI.



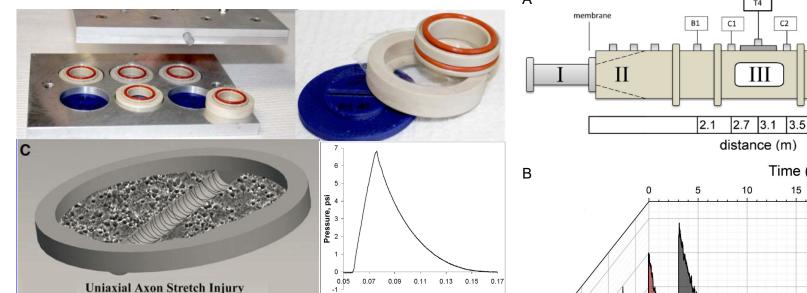
Right: Behavioral deficits in the injured ferret. (A&B) Open field activity shows injured animals spent less time in the center and more time on the perimeter of the open field box compared shams. to Movement traces shown on the right. (C&D) Animals



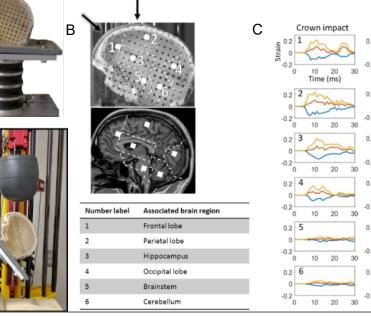
Large shock tube for ferret blast exposure. Tube has been modified to expose the ferret. A) Arrows show the testing section of the shock tube. B) Upright fixture. C) Prone fixture. A stuffed animal was used for demonstration.



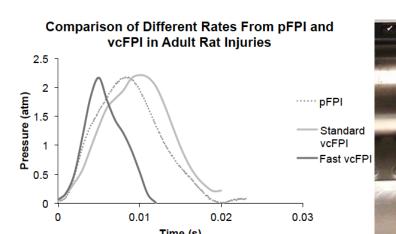
CIBM3 Shock Tubes. Top) 28" tube for human scale testing. Bottom) 9" tube for rodent testing.

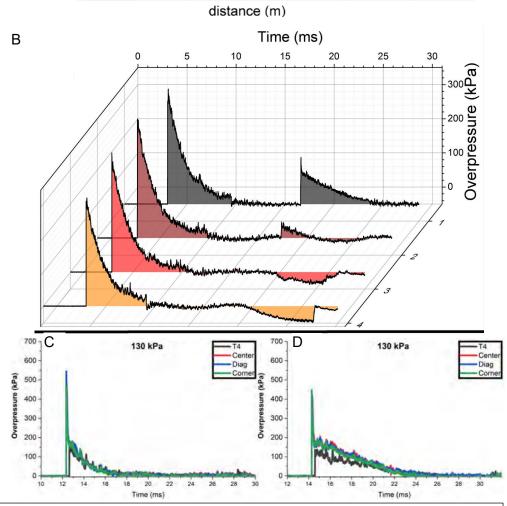


In Vitro stretch injury of cultured neurons. Study of neuronal response to high rate deformation. Allows the investigation of injury mechanisms in real time.



Human Scale Surrogate for Blunt Impact Testing. (A) Surrogate attached to a Hybrid III anthropomorphic neck with clear ballistic gel and markers for motion tracking. (B) Six brain regions of interest for spatial strain distribution. (C) Temporal strain histories for each region.





4.5

5.6

Reproduction of shock waves. (A) Schematic of shock tube. (I) an adjustable volume breech allowing adjustment of the duration and impulse, (II) variable length transition section, (III) test section equipped with bullet-proof viewing windows for high-speed video observation, and (IV) the reflector end-plate. (B) Pressure profiles showing the creation and elimination of the under pressure. (C&D) Pressure profiles showing adjustment of impulse.

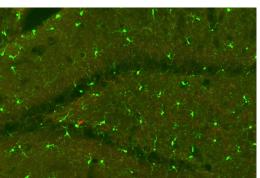
Immunocytochemistry of ferret brain. (A) Scanned hemisphere. (B) Temporal lobe and hippocampal region. (C) GFAP positive astrocytes and (D) Iba-1 positive microglia in the hippocampal region.

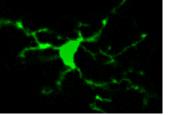
were allowed to become familiar with two objects. After injury, one object was replaced. Injured animals spent less time with the novel object than shams indicating a loss recognition.

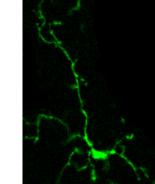
Fluid Percussion Injury (FPI) model of TBI. A custom designed linear actuated system that can deliver a fluid percussion wave representative of different TBI scenarios. System can control peak pressure, duration and impulse.

Transgenic Model for Brain Macrophages

Double transgenic model CX3CR1^{GFP/+}: CCR2^{RFP/+} mice can distinguish resident microglia from infiltrated monocytes



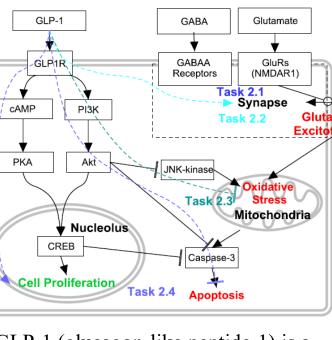




Resting (above) and activated (right) microglia cell

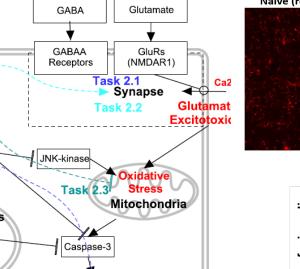


Liraglutide treatment: a GLP-1 receptor agonist

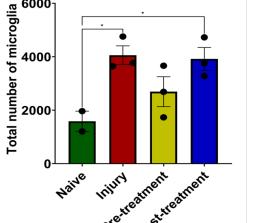


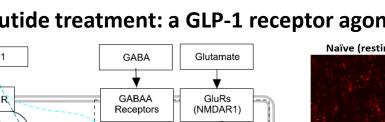
GLP-1 (glucagon-like peptide-1) is a glucose-lowering, intestinal-derived peptide with neurotrophic and anti-inflammation effects.

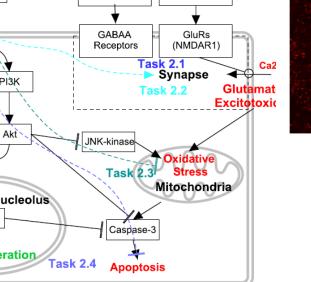




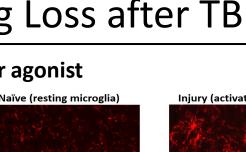
Injury (activated microglia

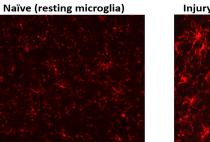


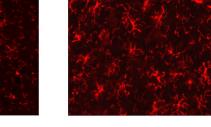


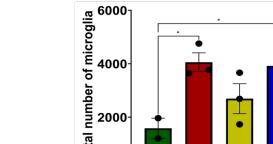


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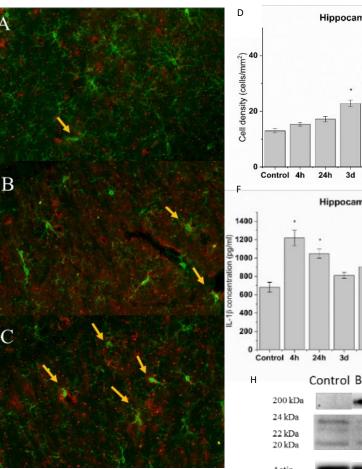






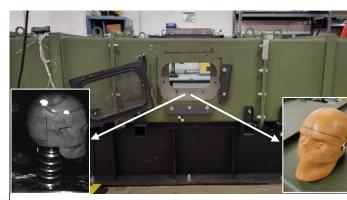
DEPARTMENT OF BIOMEDICAL ENGINEERING

Rat Model of Repetitive Blast TBI



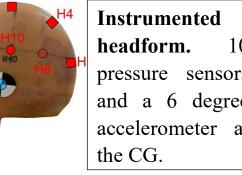
NLRP3 inflammasome activation of microglia in the hippocampus and thalamus. Animals injured at 70kPa BOP 5 times. (A-E) bTBI induces increasing NLRP3+ microglia and (F&G) related increase in IL-1β levels over 30 days post injury. (H&I) Western blot from whole brain homogenates showing cleavage of caspase 1 due to NLRP3 inflammasome activity.

Scaling TBI to the Human



Instrumented dummy head with biofidelic neck. This head has been used in the CIBM³ to determine the incident pressure acting on the head under helmeted and unhelmeted exposure to blast. Arrows show the testing section of the human scale shock tube.

H3



Intracranial headform. 10 measurements in the human head. (A-B) pressure sensors PHMS instrumented with intracranial and a 6 degree pressure sensors at five locations. D) ICP accelerometer at traces from 70kPa BOP. (E-J) ICP peaks and impulses from 70, 130, 180 kPa BOP.

