# PRE <u>Clinical Interagency reSearch resourcE-TBI</u> Preclinical Model Project



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VA Tech



## What is **PRECISE-TBI**?



## • PRE Clinical Interagency reSearch resourcE-TBI

- Mission:
  - To develop and promote an interagency resource center to accelerate development of therapies for traumatic brain injury (TBI) by elevating rigor, reproducibility, and transparency in preclinical research.

## • Resources:

- Common Data Elements,
- Open Data Commons for TBI Research (ODC-TBI)
- TBI Model Project/Model Core

Financial Support: VA ORD 150BX005878 Interagency Intellectual Support and Vision.

## **Preclinical TBI Model Project**



The mission is to improve the clinical translation of therapeutics from the "bench to bedside" by making preclinical research studies more

- Findable
  - an online preclinical catalog
  - access to model sensor
- Reproducible
  - standardized protocols to reduce the variability of model usage between laboratories.



## **Preclinical Model Project / Model Core Resources**

## • <u>Surveys</u>

- Model Information Survey
- Model Sensor Survey
- PRECISE-TBI model catalog
- Preclinical TBI protocols

**Surveys** 



ABOUT ~





## **PRECISE-TBI Preclinical Models Information Survey**

- Goal of the survey:
  - To provide the PRECISE-TBI project administration a better understanding of preclinical TBI models and information to optimize the preclinical TBI model catalog.
- Please take a few minutes to complete now



## **PRECISE-TBI Preclinical Model Sensor Survey**

## - Goal of the survey:

- This survey will give the PRECISE-TBI project administration a better understanding of how model sensors are used for TBI preclinical models.
- Please take a few minutes to complete now



# **Preclinical Model Catalog**



## What is the PRECISE preclinical model catalog?

- The catalog provides the traumatic brain injury (TBI) community with a centralized queryable online resource specific to preclinical TBI models.
- The catalog enables a more detailed search and accurate categorization of TBI article metadata (<u>https://scicrunch.org/precise-tbi</u>).





## **Model Catalog papers**

- How are **papers selected** to be added to the model catalog?
  - Curated from a multiple <u>PubMed search terms</u> from an expert in the field. Currently, there are 4 basic models being added to the catalog
    - Controlled cortical impact model
    - Fluid percussion model
    - Weight-Drop model
    - Blast model
- How is the **metadata added** to the catalog?
  - All papers in the catalog were manually curated, in preparation for future semi-automated curation process. Additional papers will be added quarterly.
- The **list of papers** that will eventually be added to the catalog is located in the <u>Preclinical TBI</u> <u>bibliography</u>.

## **PRECISE-TBI** preclinical model catalog account

- Setup to an account to access all of the features of the model catalog at https://scicrunch.org/register
  - saved searches Ο
  - access to the Application Programmatic Interface (API) An account is not required to simply view the catalog

FDI Lab: SciCrunc	h Infrastructure	INFORMATION ~ REGISTRY	COMMUNITIES	DATA LITERATURE
Home / Registration				Registration
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	Password * Confirm Password * Confirm Password * Crganization Focus to view the tooltip	9		
register	I have read the Terms and Conditions a Register Cancel	nd Privacy Policy.		⑦ Contact help desk



### https://scicrunch.org/register

## **Provide feedback or request help**

PRECISE-TBI	Model Catalog					PI	ABOUT - MY ACCOUNT -	Please leave a description of the issue and, if applicable, a
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cortical' in discovery (ks- precise-tbi-model)  Search for: "' in discovery (ks-	Dixon CE,et al., 1991	Controlled cortical impact model	rat	Sprague-Dawley	No sex reported		Beam balance test, Morris Water Maze (MWM), Beam walk test	
precise-lbi-model)  Search for: 'controlled	Manley GT,et al.,2006	Controlled cortical impact model	pig	Yorkshire	male		Intractanial P Nissi stainin B stuning (i	Send message



**Contact help** 

desk

## To the model catalog...



What species and assessments have been used for the controlled cortical injury model?

- Search for preclinical injury models in the catalog by major attributes, ė.g.,
  - Model Controlled Cortical impact Model Assessment motor, morphology

  - Species rat, mouse

What models have been used to study cognitive outcomes after pediatric mild TBI in mice?

Search for preclinical injury models in the catalog by major attributes, e.g., Assessment - motor, morphology

- Species rat, mouse Age 10-12 weeks

# Protocols

## https://scicrunch.org/precise-tbi



ABOUT ~ MY ACCOUNT ~



Model Catalog An online catalog of preclinical models of TBI Protocols Explore precinical TBI model protocols Preclinical TBI bibliography
View curated lists of preclinical TBI models

Model Sensor Survey
Provide feedback on your TBI research models

## **PRECISE-TBI Protocols**

Allow for **investigators** to **share** and **find** TBI **protocols** in a **centralized way** to encourage reproducibility in preclinical TBI research.

PRECISE-TBI protocols on Protocols.io

FAQ - protocols.io

The protocols below are created in the PRECISE-TBI workspace in Protocols.io

- ▼ Controlled Cortical Impact Model Protocol
  - Open Skull CCI in rats Available at dx.doi.org/10.17504/protocols.io.5qpvobozbl4o/v1
- ▼ Fluid Percussion Model Protocol
  - Fluid Percussion Model in rat Lyeth Lab <u>dx.doi.org/10.17504/protocols.io.rm7vzb2r5vx1/v1</u>
- Blast Injury Model Protocol
  - Open-field blast (OFB) model in mice- Available at dx.doi.org/10.17504/protocols.io.yxmvm2kwog3p/v1
  - · Advanced Blast Stimulator in rat VandeVord Lab Coming soon
- Weight-Drop Model Protocol
  - Closed Head Weight Drop Mmodel in mice Whalen Lab <u>dx.doi.org/10.17504/protocols.io.j8nlkw2pdl5r/v1</u>

## Protocols.io



Protocols.io is an **open-access repository** for **sharing** and **collaborating** on **experimental methods and protocols**.

- There are over 450 journals linked to protocols.io where authors can deposit their full protocol.
- Provides a unique, permanent identifier Digital Object Identifier, DOI, that can be cited in scholarly articles.
- Ability to modify an existing protocol, linking back to the originating protocol.
   "To ensure that the original protocol author can track reuse and receive credit for it."

# How to add a protocol to the PRECISE-TBI protocols.io community?



Working in collaboration with the PRECISE-TBI Model Catalog Team, your research group can format your protocol into the <u>Protocols.io</u> template



Abstract with PDF of publication

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ABSTRACT

This is a protocol to describe the materials and methods utilized by the submitter to perform preclinical traumatic brain injury using the open-field blast (OFB) model in mice.

Service members in theater or military training frequently are exposed to primary blast by explosive weapony. Thus, blast-induced mTBI is the most common form of TBI, regarded as a 'Signature Wound or Invisible Injury' in recent military conflicts. This highly reproducible, open-field low-intensity blast (LBI injury in mice, the "Missouri Blast" model, uses detonating 350 g of high-energy explosive Composition C-4 (C4). Open-field LB with C4, set at 1-m above the ground, generates the initial Friedlander waveform with blast rise time on microsecond scale, and includes interactions from the primary blast shockwave reflection off the ground. Comprehensive physical characterization includes the measurements of peak overpressure, blast rise time, positive phase duration, impulse, and velocity of blast waves. High-speed videography is used to capture the dynamic blast events and to ensure the reproducibility of the experimental blast exposures, confirming the absence of visible impact / acceleration on the blast-exposed mice in prone position. This model is scalable and allows study of varying magnitudes of primary blast injuries by placing animals at different distances away from the center of the blast. Overall, this animal model will provide a platform to enhance the understanding of the pathogenesis of blast-induced brain injury and is critical for developing new prevention and treatment strategies against the risk for later neurodegeneration and cognitive impairments. A list of publications using this protocol can be fround in the attached document.

The posting of this protocol is part of the mission of PReClinical Interagency reSearch resourcE-TBI (PRECISE-TBI, <u>precise-tbiorg</u>) to improve clinical translation of therapeutics by providing an online catalogue and standardized protocols to reduce the variability of model usage between laboratories.

#### BEFORE STARTING

Use and storage of explosives is governed by the Bureau of Alcohol, Tobacco, Firearms and Explosives (BAFTE) and all training and approvals should be in place before use.

#### ATTACHMENTS



Animal Prep and Animal Prep and Test Setup bind wifer at be

#### Animal Preparation

The open field environment exposes Animals to outside conditions. Hot and cold months should be avoided when planning experiments.

#### **Open-Field Blast Setup**

- 2 The open-field blast experimental site is located within the well-equipped Energetics Research Facility at Missouri University of Science & Technology, on the University Experimental Mine in Rolla.
- 3 Set the blast conditions for calculated peak overpressure using a blast simulator such as the Army Blast Effects Calculator (BEC) software or Kingery Bulmash online calculator.
- 4 Place metal mesh platforms at calculated distances away from the charge stand location allowing the blast waves to travel unimpeded in all directions. Charge stands are made for animals to be 1 meter above the ground.



Mice in prone position placed in metal mesh platforms allowing unimpeded blast wave travel

#### Induction of Primary Blast Injury

- 13 Prior to the blast experiment, anesthetize the mouse through intraperitoneal (i.p.) injection of approximately 5 µl/g body weight using a Ketamine/Xylazine mixture (25 mg/mL ketamine and 1.25 mg/mL xylazine) until it is nonresponsive to a paw or tail pinch. (NOTE: Blast exposures are conducted between 10 A.M.-12 P.M. during spring and fall seasons at the Experimental Mine). Environmental conditions need to be recorded (temperature, wind speed/direction, and humidity).
- 14 Place the animals on the positioned metal mesh platform facing the ex head and body longitudinally oriented along the direction of shock wave
- Ensure no remaining personnel are on the blast site. 15
- 16 Detonate the C4 explosive.

#### Induction of Sham Injury

20 Sham group undergo the identical procedures as the blast group only without blast loosure.

21 Once the animals are able to spontaneously move and recovery from anesthesia Intinuous 15 to 30 min.

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Injury Induction

Sham procedures

with their



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#### WIDGET

<iframe src="https://www.protocols.jo/widgets/doi?uri=dx.doi.org/10.17504/protocols.jo.yxmym2kwog3p/y1" style="width: 520px: height: 300px; border: 1px solid transparent;"></iframe>

#### QR CODE



### **BONUS: ODC-TBI allows for links to your** published protocol!

METADATA

MATERIALS METRICS

BAFTE approved blast site and explosives storage Wire mesh stands for holding animals High Frequency ICP blast pressure pencil probe for static pressure recording (e.g. PCB Model 137B25) High Frequency ICP pressure sensor for total reflected pressure (e.g. Model 102B18) Data Acquisition System (e.g. Synergy Hi-Techniques) High Speed camera (E.g. Phantom V2012) Composition C-4 (or other high explosive) Blasting cap Capacative Discharge Unit (e.g. Scorpion Blasting Machine)

#### Materials for anesthetizing:

Ketamine Xylazine Syringes (1ml) Needles (25G)



## **Data Stewardship with FAIR**



## odc-tbi.org

#### Home-cage monitoring general behavior of C57BL/6J male mice during the CognitionWall test 3 months after openfield LIB exposure

#### DOI:10.34945/F59W23

#### DATASET CITATION:

Zuckerman A., Siedhoff H. R., Balderrama A., Cui J., Gu Z. (2023) Home-cage monitoring general behavior of C57BL/6J male mice during the CognitionWall test 3 months after open-field LIB exposure. Open Data Commons for Traumatic Brain Injury. ODC-TBI:872 http://dx.doi.org/10.34945/F59W23

#### ABSTRACT:

**STUDY PURPOSE:** Evaluate the chronic-phase behavioral alterations 3 months after exposure to low-intensity blast in a home-cage-like environment during the CognitionWall test.

DATA COLLECTED: A total of 52 male C57BI/6J mice, 8 weeks old, were used. The mice were randomly allocated into one of two groups: Blast (n=29) or Sham (n=23). Mice in the Blast group were exposed to open-field low-pressure blast wave (46.6 kPa, maximum impulse of 60.0 kPa\*ms), under anesthesia. Mice from the Sham group were anesthetized but were not exposed to the blast wave. 3 months post-exposure, general behavior on the locomotor activity of the mice was measured using the PhenoTyper® home-cages (Model 3000, Noldus Information Technology, The Netherlands) and CognitionWall™ system (Noldus Information Technology, The Netherlands). All mice were familiar with the home-cage environment by being placed in the PhenoTypers for three days before conducting the CognitionWall assessments. Each mouse was housed individually, and its activity was continuously measured for 96 hours at a sample rate of 15 fps. Program-acquired data were uploaded to the web-based AHCODA-DB (Sylics, Bilthoven, The Netherlands) for meta-analysis. Eighteen behavioral parameters were analyzed and included in this dataset. See protocols and other related data in the relevant links section below.

**CONCLUSIONS:** No significant differences were found between the Blast and Sham mice in different parameters of general behavior on the locomotor activity. These data provided the essential baseline of both LIB-exposed mice and Sham controls in order to exclude the possibility that different performances in the CognitionWall tasks were caused by differences in overall locomotor activity.

## odc-tbi.org

Home / Public Data Sets /

ODC-TBI Public Dataset

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#### DATASET INFO

Contact: Gu Zezong (guze@health.missouri.edu)

Lab: PRECISE-TBI Lab: Truman Memorial VA ODC-TBI Accession:872

Records in Dataset: 5510 Fields per Record: 24

Last updated: 2023-06-09 Date published: 2023-06-09 Downloads: 4

Files: 2

#### LICENSE

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#### FUNDING AND ACKNOWLEDGEMENTS

Department of Veterans Affairs Offices of Research & Development (VA ORD) LAMb/ShEEP programs, BLR&D Director Service program UFR-002-18F, Open-Field Blast CognitionWall tasks were caused by differences in overall locomotor activity.

#### PROVENANCE / ORIGINATING PUBLICATIONS

· Chen S, Siedhoff HR, Zhang H, Liu P, Balderrama A, Li R, Johnson C, Greenlief CM, Koopmans B, Hoffman T, DePalma RG, Li DP, Cui J, Gu Z. Low-intensity blast induces acute glutamatergic hyperexcitability in mouse hippocampus leading to long-term learning deficits and altered expression of proteins involved in synaptic plasticity and serine protease inhibitors. Neurobiol Dis, 2022 Apr;165:105634, DOI: 10.1016/i.nbd.2022.105634. PMID: 35077822.. doi:10.1016/j.nbd.2022.105634.

#### RELEVANT LINKS

Home-cage monitoring spontaneous activity of C57BL/6J male mice 3 months after open-field low-intensity blast exposure

https://dx.doi.org/10.34945/F5FK5C Related dataset in ODC-TBI

NOTES

Open-field blast (OFB) model in mice protocol

https://dx.doi.org/10.17504/protocols.io.yxmvm2kwog3p/v1 Protocol for the Open-field blast (OFB) model in mice in protocols.io

Open-field Blast parameters dataset

https://dx.doi.org/10.34945/F5630G Datasets with the blast parameters for the relevant subjects

Service, Columbia, Missouri, USA; Department of Pathology and Anatomical Sciences, University of KEYWORDS Cross-linked to papers Missouri School of Medicine, Columbia, Missouri School of Medicine, Columbia, Missouri USA: Department of

Service, Columbia, Missouri, USA; Department of Pathology and Anatomical Sciences, University of Missouri School of Medicine, Columbia, Missouri, USA Cui, Jiankun

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👌 PRECISE-TBI | Searching for blast model

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https://scicrunch.org/precise-tbi/discovery/source/ks-precise-t...

**Open-field blast model** (Chen S. et al.,2022)

Asociated Protocols: 6040

Asociated Datasets: 6041

TBI Model Type: Blast model

Organism Species: mouse

Organism Strain: C57BL/6J

**Assessments:** mEPSCs, home-cage monitoring (HCM), CognitionWall, label-free quantitative proteomics, STRING Protein interaction

**Citation:** Chen S, Siedhoff HR, Zhang H, Liu P, Balderrama A, Li R, Johnson C, Greenlief CM, Koopmans B, Hoffman T, DePalma RG, Li DP, Cui J, Gu Z.Low-intensity blast induces acute glutamatergic hyperexcitability in mouse hippocampus leading to long-term learning deficits and altered express ...[more]

Asociated Protocols: DOI:10.17504/protocols.io.yxmvm2kwog3p/v1

Asociated Datasets: DOI:10.34945/F59W23



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## **User Experience Feedback!**

5-star customer service

Very User Friendly

Prompt Feedback

Very important initiative to help increase rigor and reproducibility!



## Contact us at modelcore@precise-tbi.org



Preclinical TBI Model Sensor Survey (v 1.0)				
	PR	ECISE-TBI		
Name and Institution				
TBI Model (e.g., flui	d percussion, CCI, blast, weight drop)			
Sensor Type (check one or more)				
Pressure tran	sducer		Make and Model number	

# Visit our booth to take the survey and learn more about PRECISE-TBI!

AD Card	Make and Model number
Software	Make and Model number
Other equipment	Make and Model number
Sensor use (check all that apply)	
Calibration	
For each experiment	
Both	

## Thank you!!!

## Slides from this workshop will be posted to link on NINDS TBI website



https://www.ninds.nih.gov/current-research/focusdisorders/focus-traumatic-brain-injury-research

