

Developing and using Preclinical TBI CDEs to Share Data in the TOP-NT* Consortium

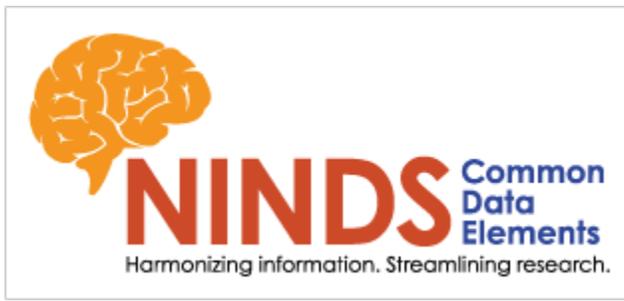
*Translational Outcomes Project in Neurotrauma



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NINDS Translational Outcomes Project in Neurotrauma (TOP-NT)- UH-3 Grant



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Extramural Programs



- Bring together a collaborative, multidisciplinary team
- Use non-invasive in vivo measures; have direct clinical applicability
 - Serum Biomarkers and Imaging
- Create requisite Data Dictionary, CDEs, SOPs
- Internal Validation with different methodologies (measurements)
- Construct Validation matching preclinical and clinical TBI
- Utilize 3 TBI models
- External Validation with reproducibility across sites
- Share the data; odc-tbi – Open Data Commons for Data Sharing
- Utilize FAIR Principles → Data Sharing & Analytics



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TBI Models

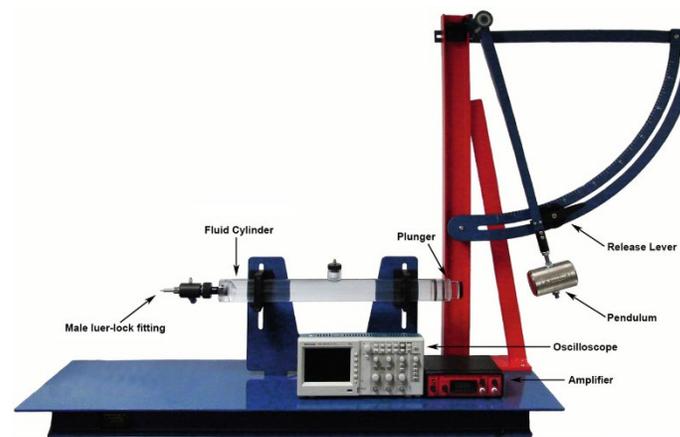
Contusion: Controlled Cortical Impact

Diffuse trauma: Lateral Fluid Percussion Injury model

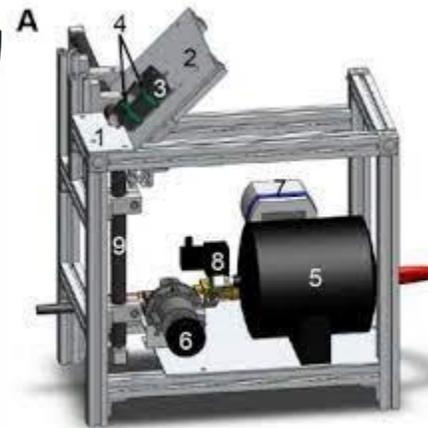
Rotational acceleration: CHIMERA (Closed-Head Impact Model of Engineered Rotational Acceleration)



CCI (2 levels)



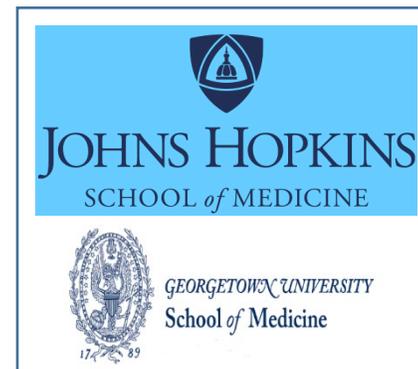
FPI



CHIMERA



Charles River Sprague-Dawley
(001CD, 180-220g, ♀♂)



General Procedures

Example—Contusion Injury: Controlled Cortical Impact

- Six days acclimation and handling in animal facility after delivery
- Power analyses prior to study/randomization
- Study: 12, 4-rat cohorts (2 ♀ 2♂, one each CCI or Sham, \bar{x} 65 days old)
- Day 0: CCI/Sham (24 rats/group), vaginal smear
- Day 1: Serum tail vein 500 μ l, rotarod (baseline collected Day -3)
- Day 3: Y-maze, serum, MRI
- Day 7: Serum
- Day 29: Elevated zero maze
- Day 30: Y-maze, MRI, CSF and serum, euthanasia

Creation of a Data Dictionary

Site	Variable Name	Title	Element Type	Domain	Comments	Description
A	B	C	D	E	F	G
Creating Site	VariableName	Title	Element Type	Domain	Comments	Description
UCLA-UF	Site	Site	TOP-NT_CDE	General		Experimental Site
UCLA	AnimalGeneModTxt	Animal genetic modifications text	Common Data Element	General-animal	All animals in this study were wild type and contained no gene modifications	A free text describing animal genetic modification(s)
UCLA-UF	AnimalAgeVal	Experimental age	Common Data Element	General-animal		Age of the animal (in months) at the time of test
UCLA-UF	AnimalBirthDate	birth date	Common Data Element	General-animal		Date (and time, if applicable and known) the animal participant/subject was born
UCLA	LightCycleTimeDur	Light Cycle time Duration	Common Data Element	General-animal	Record the duration of light cycle per day	
UCLA	LightDarkCycleTyp	Light/Dark cycle type	Common Data Element	General-animal	normal is : 12 light hours and 12 dark hours	reversed or not reversed=normal
UCLA	RandomInd	Randomization indicator	Common Data Element	General-animal		
UCLA	RandomizationMethTxt	method for randomization	Common Data Element	General-animal	Record how experimental groups were randomized	
UCLA-UF	AnimalHousingTyp	Animal subject housing type	Common Data Element	General-animal	All animals were housed in pairs of 2 per cage (group).	Type of animal subject pre-injury housing including individual or group housing
UCLA-UF	AnimalSexTyp	Animal sex type	Common Data Element	General-animal		Type of animal species sex as determined by observation
UCLA-UF	AnimalSpeciesTyp	Animal species type	Common Data Element	General-animal	All animals in this study were rats.	Type of animal species being studied.
UCLA-UF	AnimalSmallStrainTyp	Small animals - strain type	Common Data Element	General-animal	All rats in this study were Sprague-Dawley	Type of the small animal strain (for mice and rat)

Summary of CDEs

Translational Outcomes Project in Neurotrauma CDE domain alignment

477 TOP-NT CDEs

New TOP-NT (268)	Endorsed by TOP-NT (209)	Adopted unchanged (172)	TOP-NT modified (37)
	Preclinical (LaPlaca et al.) 132	123	9
General, Animal (3, 2 of which also MRI)	General, animal	15	
General, Injury (39)	General, injury	53	4
Behavior (18)	Behavior	55	5
	Clinical (FITBIR) 77	49	28
MRI (119)	FITBIR	MRI (56)	7
Biomarkers (22+5 see histopath =27)	BRICS	Biomarker (23)	18
Histopathology (69, 5 of which also Biomarkers)		Histopathology all FITBIR (8)	8 (5 also MRI, 2 also biomarkers)
	Neuropathology	Histopathology	4 (3 are also MRI)

Pre-Clinical Common Data Elements
for Traumatic Brain Injury Research:
Progress and Use Cases

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Open Data Commons for Traumatic Brain Injury
odc-tbi.org

3 of the MRI are also aligned with Neuropathology CDEs
5 are modified histopath and MRI



Data Compiled and Slide prepared by Ina Wanner, UCLA

TOP-NT Consortium

- Overall plan—cooperative strategy
 - Biweekly meetings; detailed SOPs, CDEs
 - Consortium MTAs; Pub. Policy/authorship agreements
 - Harmonization: TBI models devices, MRIs, Standardization
 - Primary outcomes: MRI and biomarkers
 - Validation: Match MRI and neuropathology and behavior
 - Design: Injury x Sex x Center x Timepoints
- Six University SOMs
 - Element Dictionary: 477 terms
 - 17 Datasets (Injury Model, Biomarkers, MRI, Neuropathology, Behavior)
 - >1,000 mice and rats
 - >2 million data points

Translational Outcomes Project in Neurotrauma TOP-NT Consortium

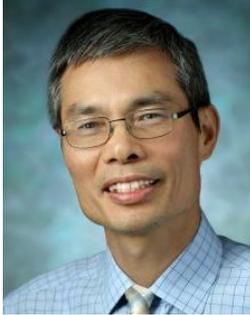
TOP - NT groups



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Neurological Disorders
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Jiong Liu
Anyu Fan
Laura Tucker

Adam Ferguson

Austin Chou

Susanna Rosi, Jaqueline Bresnahan, Michael Beattie

UCSF



Monday TOP-NT Posters:

Allende Labastida et al. JHU P04.023

Tuesday TOP-NT Posters:

Wanner UCLA P04.301

Vichare/Allende Labastida UCLA/Hopkins PS04.314

Myers UCLA P04.316



Wednesday 6/28 lunch Workshop:

Ray Koehler & Ina Wanner

*Data and Analysis Techniques to Improve
Rigor in Preclinical Neurotrauma*

11:45 am to 1:15pm

Thank you



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