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

*Translational Outcomes Project in Neurotrauma

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The opinions, interpretations, conclusions and recommendations are those of the authors and are not necessarily endorsed by the U.S. Army, Department of Defense, the U.S. Government or the Uniformed Services University of the Health Sciences, or the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. The use of trade names does not constitute an official endorsement or approval of the use of reagents or commercial hardware or software. The authors declare no conflicts of interest.
NINDS Translational Outcomes Project in Neurotrauma (TOP-NT)- UH-3 Grant

- 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
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 500µl, 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

<table>
<thead>
<tr>
<th>Site</th>
<th>Variable Name</th>
<th>Title</th>
<th>Element Type</th>
<th>Domain</th>
<th>Comments</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCLA</td>
<td>AnimalGeneModTxt</td>
<td>Animal genetic modifications text</td>
<td>C</td>
<td>Common Data Element</td>
<td>All animals in this study were wild type and contained no gene modifications</td>
<td>A free text describing animal genetic modification(s)</td>
</tr>
<tr>
<td>UCLA</td>
<td>AnimalAgeEval</td>
<td>Experimental age</td>
<td>D</td>
<td>Common Data Element</td>
<td>Age of the animal (in months) at the time of test</td>
<td>Date (and time, if applicable and known) the animal participant/subject was born</td>
</tr>
<tr>
<td>UCLA</td>
<td>AnimalBirthDate</td>
<td>birth date</td>
<td>E</td>
<td>Common Data Element</td>
<td>Date of experiment</td>
<td>Date of experiment</td>
</tr>
<tr>
<td>UCLA</td>
<td>LightCycleTimeDur</td>
<td>Light Cycle time Duration</td>
<td>F</td>
<td>Common Data Element</td>
<td>Record the duration of light cycle per day</td>
<td>normal 12 hours and 12 dark hours; reversed or not reversed=normal</td>
</tr>
<tr>
<td>UCLA</td>
<td>RandomInd</td>
<td>Randomization indicator</td>
<td>G</td>
<td>Common Data Element</td>
<td>Record how experimental groups were randomized</td>
<td>Record how experimental groups were randomized</td>
</tr>
<tr>
<td>UCLA</td>
<td>AnimalHousingTyp</td>
<td>Animal subject housing type</td>
<td>H</td>
<td>Common Data Element</td>
<td>All animals were housed in pairs of 2 per cage (group),</td>
<td>Type of animal subject pre-injury housing including individual or group housing</td>
</tr>
<tr>
<td>UCLA</td>
<td>AnimalSexTyp</td>
<td>Animal sex type</td>
<td>I</td>
<td>Common Data Element</td>
<td>All animals in this study were rats</td>
<td>Type of animal species as determined by observation</td>
</tr>
<tr>
<td>UCLA</td>
<td>AnimalSpeciesTyp</td>
<td>Animal species type</td>
<td>J</td>
<td>Common Data Element</td>
<td>All animals in this study were Sprague-Dawley</td>
<td>Type of animal species being studied</td>
</tr>
<tr>
<td>UCLA</td>
<td>AnimalSmallStrainTyp</td>
<td>Small animals - strain type</td>
<td>K</td>
<td>Common Data Element</td>
<td>All rats in this study were Sprague-Dawley</td>
<td>Type of the small animal strain (for mice and rat)</td>
</tr>
</tbody>
</table>
## Summary of CDEs

### Translational Outcomes Project in Neurotrauma CDE domain alignment

**477 TOP-NT CDEs**

<table>
<thead>
<tr>
<th>Domain</th>
<th>Adopted unchanged (172)</th>
<th>TOP-NT modified (37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preclinical (LaPlaca et al.)</td>
<td>123</td>
<td>9</td>
</tr>
<tr>
<td>General, animal</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>General, injury</td>
<td>53</td>
<td>5</td>
</tr>
<tr>
<td>Behavior</td>
<td>55</td>
<td>5</td>
</tr>
<tr>
<td>Clinical (FITBIR)</td>
<td>49</td>
<td>28</td>
</tr>
<tr>
<td>FITBIR</td>
<td>49</td>
<td>7</td>
</tr>
<tr>
<td>MRI (56)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRICS</td>
<td></td>
<td>18</td>
</tr>
<tr>
<td>Biomarker (23)</td>
<td></td>
<td>8 (5 also MRI, 2 also biomarkers)</td>
</tr>
<tr>
<td>Histopathology all FITBIR (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuropathology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histopathology</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### New TOP-NT (268)
- Endorsed by TOP-NT (209)
- Adopted unchanged (172)
- TOP-NT modified (37)

### Additional Information
- MRI (119)
- Biomarkers (22+5 see histopath =27)
- Histopathology (69, 5 of which also Biomarkers)
- 3 of the MRI are also aligned with Neuropathology CDEs
- 5 are modified histopath and MRI

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Data Complied 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
Thank you

Marcello Febo, Professor and Director of Translational Research Imaging Departments of Psychiatry and Neuroscience University of Florida College of Medicine, Gainesville, FL

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