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Pre-Clinical Models of Penetrating Brain Injury: Study Protocol for a Systematic Review

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OBJECTIVES/GOALS: Penetrating brain injury (PBI) differs both physiologically and in clinical outcomes when compared to blunt-force traumatic brain injury (TBI). Despite this, there are few pre-clinical models of PBI described in the literature. To address this gap, we will develop a study protocol for a systematic review. METHODS/STUDY POPULATION: Three electronic databases (PubMed, Embase, Web of Science) will be searched using keywords and controlled vocabulary related to animal models, computational models, simulations, and disease key words including traumatic brain injury and penetrating brain injury. The primary outcome will be the method of PBI modeling. Secondary outcomes will be related to bibliographic information, computational analysis, and histochemical, radiographic, behavioral, and human clinical biomarkers and outcome measures used in PBI models. A panel of independent investigators will review publications resulting from this search strategy to identify relevant studies. The protocol will adhere to PRISMA-P guidelines. RESULTS/ANTICIPATED RESULTS: Eligible studies will include both exploratory and descriptive research, and both quantitative and qualitative data. A summary of selected studies will be presented, and the synthesis will follow a narrative framework. DISCUSSION/SIGNIFICANCE: This protocol provides a framework for comprehensively evaluating pre-clinical PBI models with focus on methodology. PBI is a phenotypically unique disease and is under studied. This protocol will be of great benefit to clinicians and scientists in this emerging field and can help monitor future progress in translational research.

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The brain under stress: How a history of unpredictable shock affects neural processing of future stressors

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OBJECTIVES/GOALS: Determine how a history of unpredictable foot shock in mice affects brain wide patterns of neural activation to future stressors. Additionally, we aimed to characterize how the paraventricular nucleus of the thalamus (PVT) is involved in the fear sensitization process. METHODS/STUDY POPULATION: We used a mouse model of stress enhanced fear learning, where stressed mice are first subjected to a series of unpredictable foot shocks in a novel context while control mice undergo exposure to the novel context without experiencing foot shock. Mice are then left undisturbed for 28 days, following which they are exposed to a single foot shock in a novel context. Mice are tested in the second context 24 hours after single shock, and the amount of time spent frozen in the context provides a measure of fear sensitization. Whole brain patterns of activation during the second context test will be assessed via whole brain optical clearing with antibody staining of immediate early genes. The role of the PVT in fear sensitization will be characterized using chemogenetic approaches. RESULTS/ANTICIPATED RESULTS: Our preliminary results demonstrate that mice display enhanced fear acquisition long after the initial experience of unpredictable shocks. We anticipate to identify regions previously implicated in fear learning and novel regions not previously described through our brain clearing approach. In addition, we anticipate chemogenetic inhibition of the PVT will reduce freezing to an auditory cue associated with the shock in the second context but not to the context itself. DISCUSSION/SIGNIFICANCE: Our findings will provide a comprehensive view of how a history of unpredictable stress affects whole brain processing of subsequent stressful experiences, and describe the role of the PVT in cued fear sensitization.

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Operationalization of a Translational Ethics Program

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OBJECTIVES/GOALS: Within our CTSA hub, greater emphasis is on understanding innovation and human health impact of translational science writ large rather than focus on translational research projects. Our program is restructured to reflect distinguishing ethical features of translational science which are complimentary to traditional research ethics issues. METHODS/STUDY POPULATION: This descriptive analysis depicts the development of our ethics program as an exemplar of how to integrate into the research enterprise of an academic health science center that engages in translational research. Our relational approach is predicated on the embodiment of ethical values by all who are involved in research committed to proactive dialog, team building, and collaboration. This translational research culture is facilitated by a multidisciplinary ethics team who are embedded throughout the translational research enterprise. RESULTS/ANTICIPATED RESULTS: Our program is integrated into a translational science enterprise within a CTSA hub in four areas: relational structure (from leadership team to community engagement), education (from trainees to the research community to the public), support (through ethics consultation with multiple touchpoints in the translational science pathway), and team science (from team on-boarding and communication to D&I research of team science interventions). We have developed a research agenda examining research ethics topics that increase quality, applicability and downstream social impact of research; understanding translational science through historical and science & technologies studies lenses, and ethnographic and mixed-method approaches to understanding team science and the science of team science. DISCUSSION/SIGNIFICANCE: The integration of a translational ethics program provides attention to traditional research ethics issues regarding study conduct and integrity but also transcends those concerns to focus on the translational science enterprise itself through relationships, cultivating trust, team science, DEIA, and social responsibility.

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Pathophysiology of voluntary motor commands in patients with multiple sclerosis identified using reverse engineering of motor unit population discharge.

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OBJECTIVES/GOALS: Our objective is to characterize excitatory, inhibitory, and neuromodulatory components of the voluntary

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