Lower Motor Neuron Degeneration Following Traumatic Brain Injury

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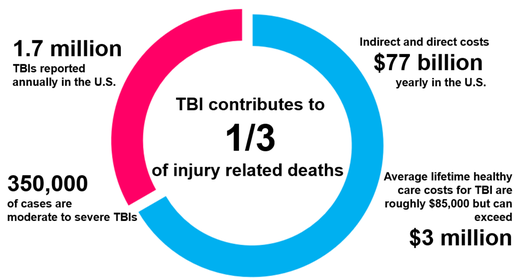
Introduction

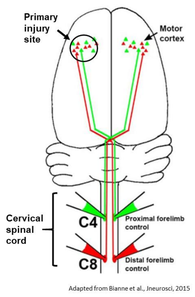
A traumatic brain injury (TBI) is defined as an injury to the head that disrupts the normal function of the brain[2]. In 2013 alone, there were approximately 2.8 million TBI related emergencies reported in the United States consisting of ~2.5 million emergency room visits, 282,000 hospitalizations, and 56,000 deaths[1].

Primary injuries of TBI result in immediate cell death and disruption of normal functionality. Presently, there are no standardized treatments or cures for a TBI primary injury besides symptomatic treatments and supportive therapies. Secondary injuries however result in a complex biochemical process that can lead to cognitive impairments[2] and a greatly increased risk for the development of several chronic neurodegenerative disorders[3]. In this sense, TBIs can be described as a disease process that only begins with the primary injury.

Currently there is some debate as to the role of TBIs and the future development of motor neuron diseases (MNDs) such as amyotrophic lateral sclerosis (ALS). In this study, we plan to analyze the relationship between a TBI and the development of MNDs using immunohistochemical markers of proteinopathies in a post TBI animal model.



Objective

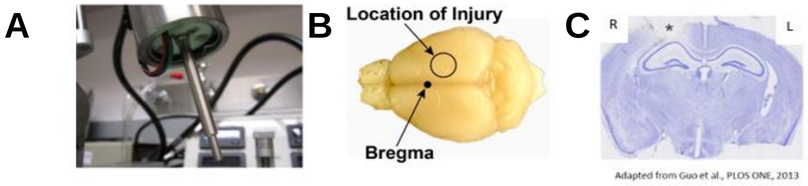


Adapted from Bianne et al., Jneurosci, 2015

The goal of this research project is to explore the effects of a single traumatic brain injury (TBI) on lower motor neuron (LMN) loss and degeneration as detected with TDP-43 pathologies. The primary injury site of the TBI is focused on the primary motor cortex of the brain. Specific motor neurons of this area primarily send neural impulses to the cervical spinal cord that controls proximal and distal forelimb motor control. The cervical spinal cord is functionally connected to the motor cortex that is injured, therefore providing the opportunity to study downstream neurodegenerative effects.

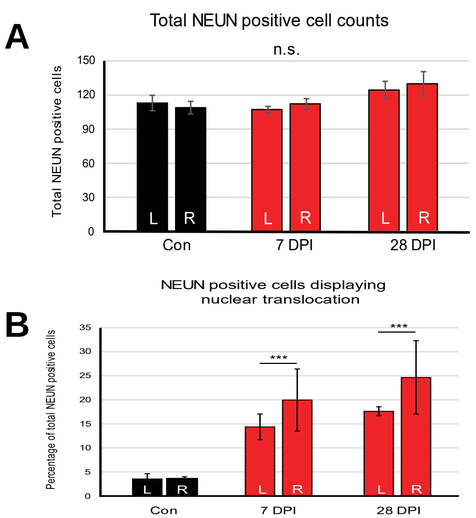
Experimental Methods

The current preliminary data was collected from wild-type C57BL/6J mouse cervical spinal cords. Injuries were performed using a stereotaxic mounted impactor centered over the primary motor cortex of the right cortical hemisphere after performing a 3mm diameter craniotomy. Injury impact was controlled at 2mm diameter X 1mm depth for mice. Following TBI and recovery, animals were sacrificed at specified time points by transcardial perfusion with ice-cold PBS followed by ice-cold 4% PFA. Spinal cords were dissected and prepared for immunohistochemical analysis.



A) Electromagnetic impactor device with impactor tip inserted. B) Representative image of the placement of the craniotomy and injury site in a C57BL/6J mouse brain. C) Cross-section showing the resulting damage of the TBI injury in a C57BL/6J mouse cortex.

Preliminary Analysis – Nuclear Mislocalization

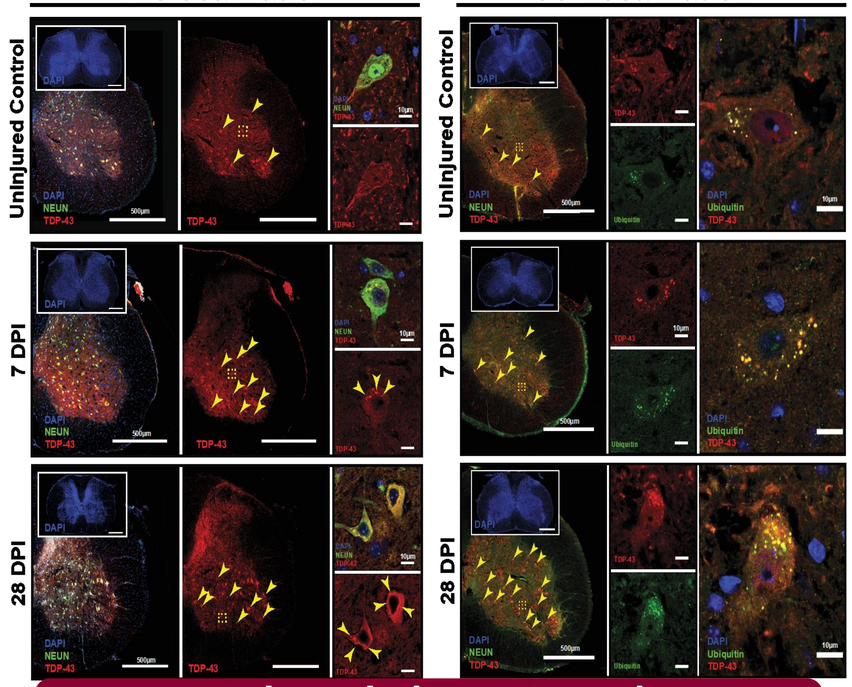


A) **Total NEUN positive cell counts. This suggests that there is no statistically significant difference of NEUN positive cell counts between control and TBI mice.**

B) **NEUN positive cells displaying nuclear translocation. This suggests that there is a statistically significant increase in those cells in the injured animals. The counts were performed both ipsilateral (R) and contralateral (L) to the cortical injury site. There were no statistically significant differences between the number of affected neurons within the two spinal cord hemispheres.**

TDP-43 Nuclear Mislocalization/Ubiquitination

C7 and C8 Cervical Spinal Cord



Acknowledgments and References

This work was funded by Fulton Undergraduate Research Initiative (FURI). Special acknowledgment goes to Dr. George Bjorklund for providing guidance and mentorship.

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