TRAUMATIC BRAIN INJURY AND CHRONIC VARIABLE STRESS IN ADOLESCENTS

Macy Urig

University of Cincinnati

urigmr@mail.uc.edu

Hello, My name is Macy Urig and I am from the University of Cincinnati. Today I will be discussing traumatic Brain Injuries and chronic variable stress in adolescence

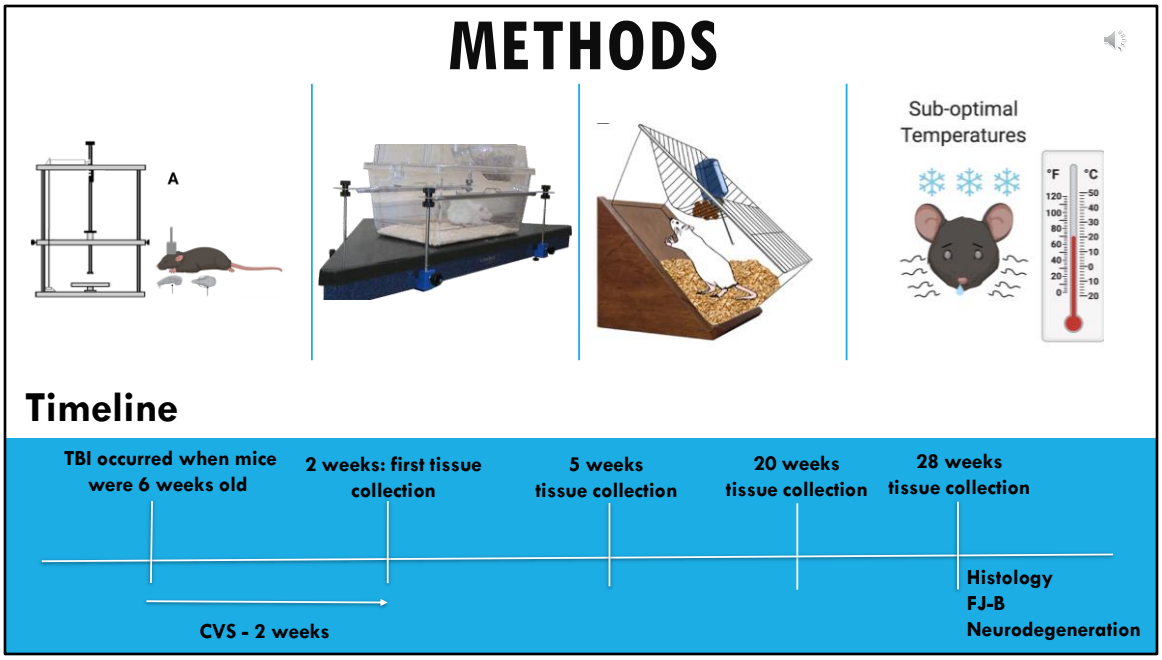
BACKGROUND

- Approximately 30% of adolescents report that daily life activities are affected when they are overly **stressed**.
- Adolescents have the **second highest rate of TBI.**
  - 2nd to the geriatric population

Adolescence are pretty stressed these days, am I right? This has been even more true over the past two years with the current state of the world. Approximately 30% of adolescence said that their sleeping, eating and exercise habits change when they are overly stressed, and due to the inherent vulnerability of this developmental stage, it is no surprise that adolescents are at an increased risk of worse outcomes from illness when also experiencing chronic stress. One of these chronic illnesses can include traumatic brain injury, or TBI. Roughly 1 million adolescence acquire a TBI annually. Currently, there is no data to show the affects that stress has on the recovery from a TBI.

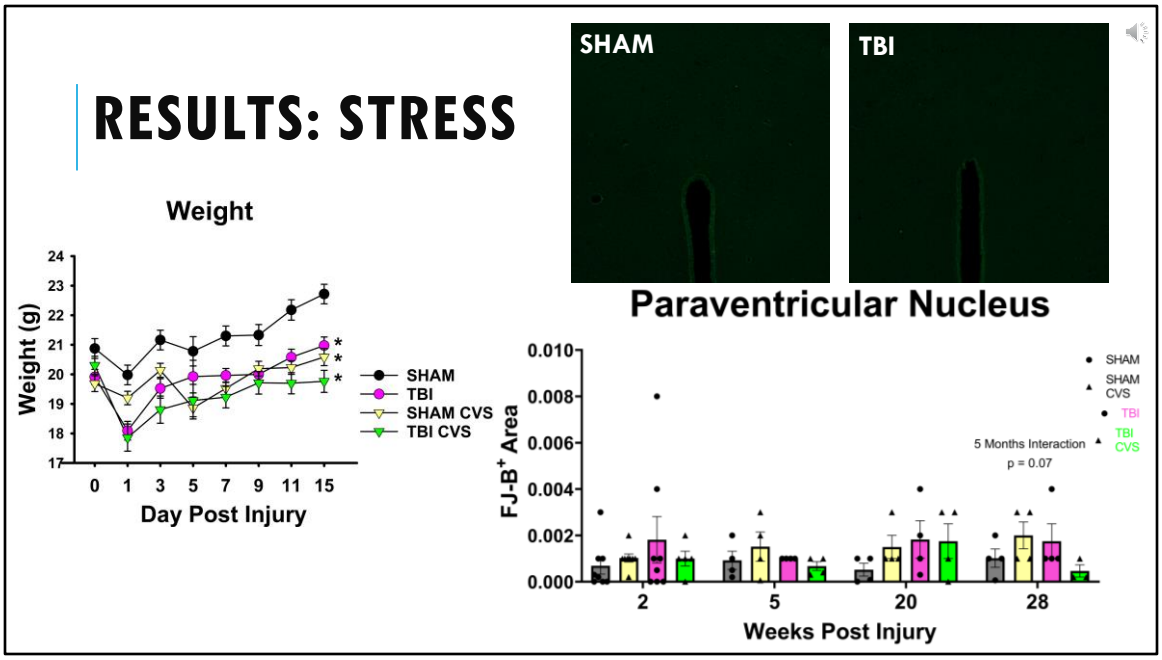
HYPOTHESIS

We hypothesize that chronic variable stress will worsen histological outcomes of TBI.



TBI (@6 weeks) -> chronic variable stress for 2 weeks -> 2 week mice euthanized-> 5 weeks -> 20 week-> 28 weeks

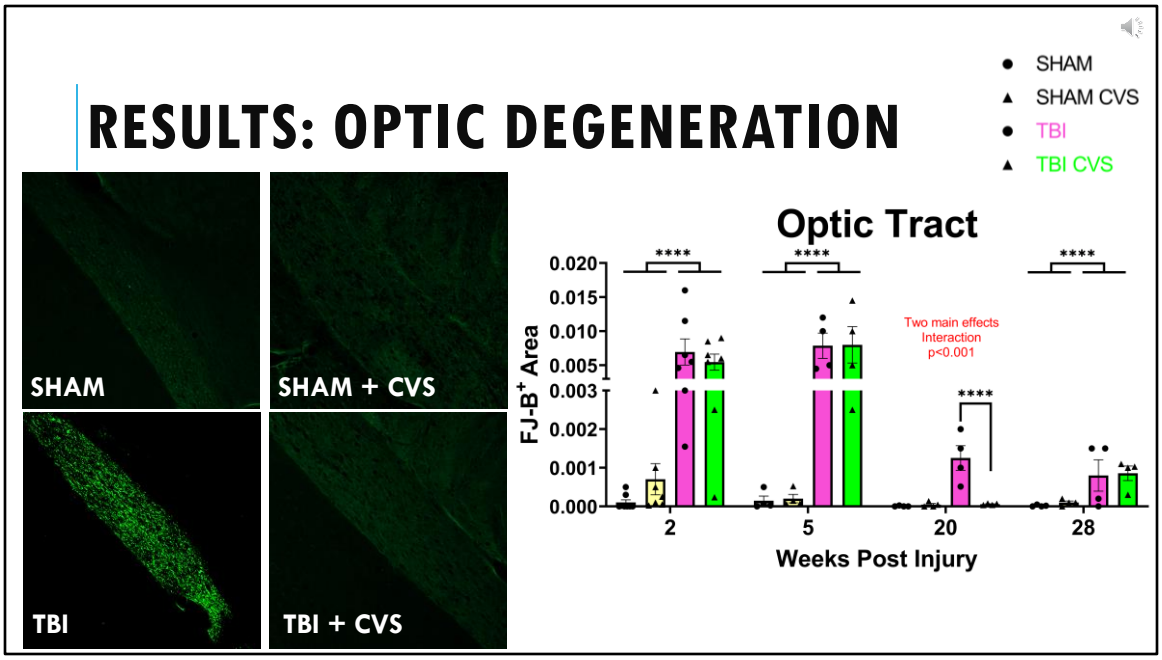
The general timeline for our study followed as such. 6-week-old male c57/bl6 mice were anesthetized and experienced a closed-head weight drop TBI roughly above bregma (depicted in the first left image) or sham/no injury. After TBI, mice were exposed to 2 weeks of chronic variable stress including stressors like, cage tilt, hypothermia, or wet bedding occurred leading to the first tissue collection at 2 weeks. The following tissue collections occurred at 5,20 and 28 weeks. After tissue collection the brains were analyzed using Floro-jade B



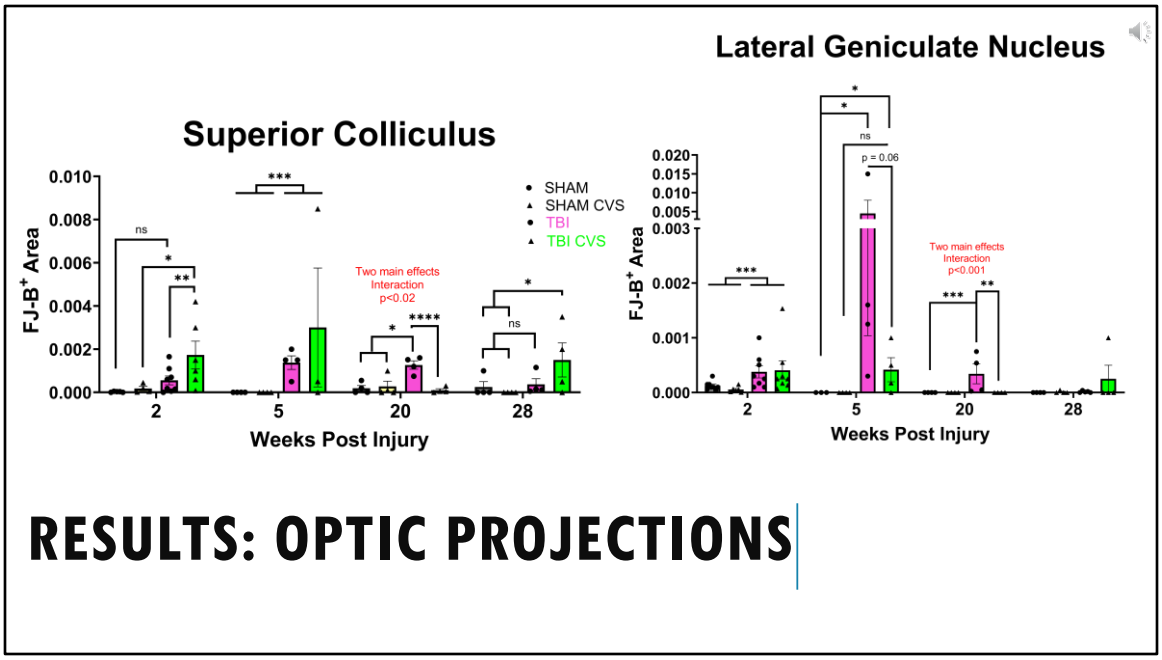
First, we confirmed whether there was a stress effect and then examined brain tissue for neurodegeneration in stress-associated regions.

We confirmed a stress effect by recording weight loss throughout the duration of CVS and showed that even uninjured mice that underwent stress weighed significantly less than sham mice, and injured mice whether stressed or not also weighed less than sham.

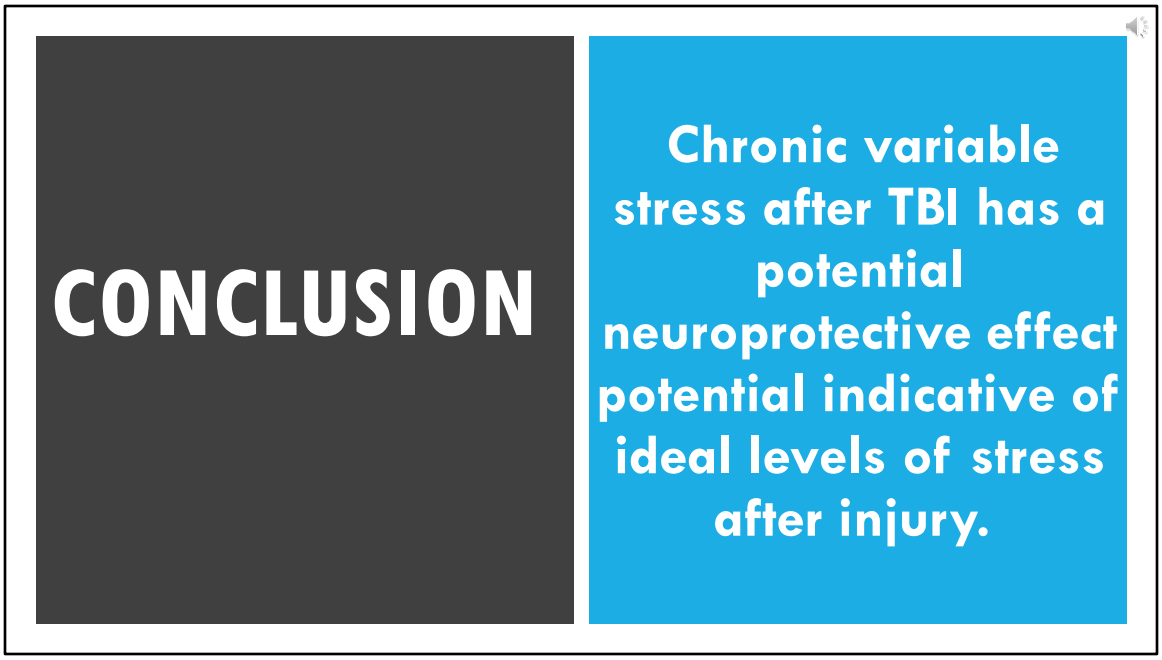
We examined the brain for degeneration in stress-associated regions like the Paraventricular Nucleus, which is a hypothalamic stress pathway-integration hub, we saw no positive staining as shown in these images. In fact, the signals you see in the graph are only background as there was nothing to be measured.



I should note that our TBI model has been characterized as a traumatic optic neuropathy model because degeneration is predominantly localized to optic regions, so when determining whether stress had any affects on injury outcomes, we decided to focus on optic regions like the optic tract, shown here. As you can see in the images, it is clear that the sham, CVS, and CVS + TBI groups are all very similar, but at 20 weeks, there is a considerable amount of degeneration in only the injured group not given CVS. This is degeneration in the optic tract. This was supported when we found a significant interaction at 20 weeks, but this effect was interestingly not seen at any other time point.



This CVS effect remained true for optic projection regions at 20 weeks including the brain stem superior colliculi and the thalamic lateral geniculate nucleus.
While lateral geniculate data largely follows optic tract degeneration across the time course, the superior colliculi seems more vulnerable to TBI + CVS showing significantly more degenerating axons at 2 and 28 weeks. This unexpected protective effect of CVS at 20 weeks is perplexing and certainly warrants further studies to determine which factors might explain these data points. For example, we are currently examining these regions for dysfunctional glial cells which our lab has shown in the absence of stress are reactive dependent on time after injury. Understanding how other cell types respond to axonal injury and stress may reveal not only why 20 weeks in a critical time point, but why the superior colliculi is more vulnerable. Perhaps this region is taxed more during stress or perhaps it takes longer for protective mechanisms to arrive at this further location.



In conclusion, chronic variable stress after TBI was seen to have a neuroprotective effect, at least at 20 weeks. Since at 2 weeks the data was consistent between both the TBI and TBI +CVS data _____

ACKNOWLEDGEMENTS

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