A novel approach for assessing traumatic brain injury induced light aversion in mice.

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Introduction

- Traumatic Brain Injuries (TBIs) can cause functional and structural damage to the optic tract and other pathways involved with vison.[1,2]
- Our lab has shown that damage to these pathways leads to visual deficits, observed as a decline in the optokinetic response (OKR).[3] This is an involuntary response whereby the eyes (or a mouse's whole head) will follow moving stimuli.
- Studies show that 50% of individuals who have experienced a TBI also suffer from photalgia, or abnormal light aversion, when exposed to bright light.[4]
- Photalgia is associated with cell loss in the retina, which we see in our TBI model.[3]
- In order to detect deficits in cognitive, motor, and visual processes after a TBI, eye movement dysfunction is a commonly used tool; however, no one has used this to examine light aversion in mice to date.[5]

Hypothesis

Following a TBI, we hypothesize that damage to the visual system increases photalgia, which will be seen through more severe optokinetic deficits at higher light intensities.

Methods

Animals
8-week-old adult male C57Bl/6J mice

Traumatic Brain Injury
Closed head weigh drop model (Fig. 1a)
A 400 g weight was dropped 1.5 cm above bregma in anesthetized mice.

Optokinetic Behavior Testing
Our OKR device (Fig. 1c) was adapted to produce an unpleasant visual environment with 4 different light intensities (80 lux, 400 lux, 1100 lux, and 3200 lux). Mice were placed on an elevated platform in the center of the device with no restriction on movement and recorded for 1 minute per light. Mice were tested with a variety of visual gratings (to assess visual acuity) at multiple times after injury (Fig. 1b).

Statistical Analysis
GraphPad Prism
2way ANOVA

Results

Figure 1

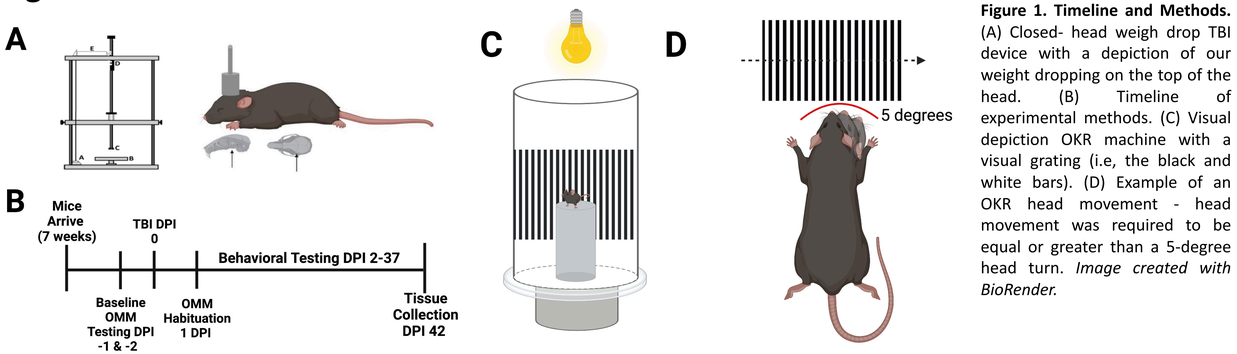

Figure 1. Timeline and Methods. (A) Closed- head weigh drop TBI device with a depiction of our weight dropping on the top of the head. (B) Timeline of experimental methods. (C) Visual depiction OKR machine with a visual grating (i.e, the black and white bars). (D) Example of an OKR head movement - head movement was required to be equal or greater than a 5-degree head turn. *Image created with BioRender.*

Figure 2

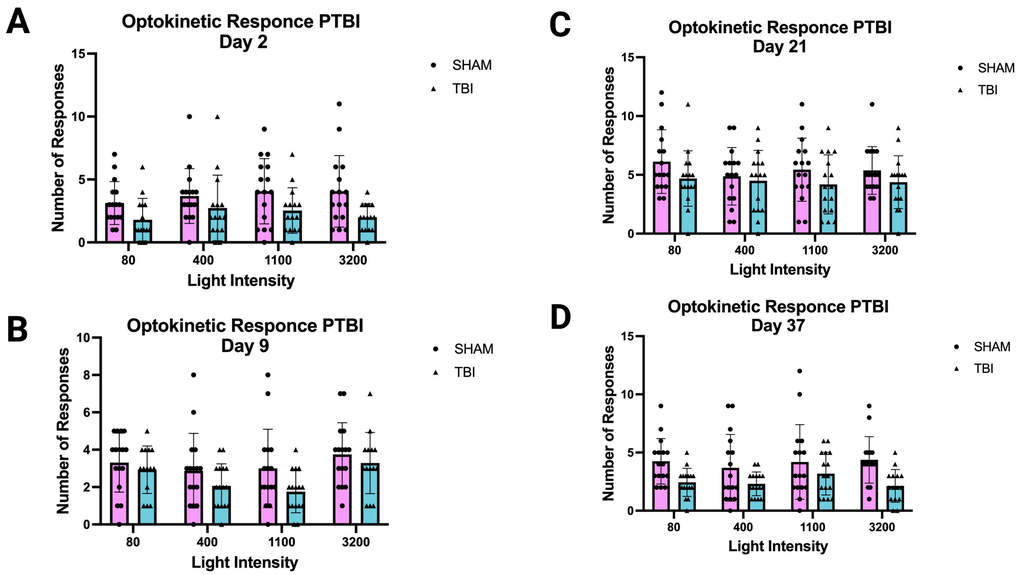

Figure 2. Light aversion Analysis and Optokinetic Analysis. (A) Optokinetic Response Post TBI (PTBI) Day 2 shows a main effect of injury (p= 0.0011), where sham mice produced more OKR compared to TBI mice. (B) Optokinetic Response PTBI Day 9 shows a main effect of light (p= 0.0125) and injury (p= 0.0394), where sham mice produced more OKR compared to TBI mice. However, sham and TBI mice produced the most OKR in 3200 lux, which is the brightest light intensity condition given. (C) Optokinetic Response PTBI Day 21 shows a main effect of subject (p= 0.0025), where each individual mice performed differently from their counterparts regardless of light or injury. However, post-hoc analysis revealed no further significant results at this time point. (D) Optokinetic Response PTBI Day 37 shows a main effect of injury (p= 0.0025), where sham mice produced more OKR compared to TBI mice.

Discussion/Conclusions

- Injured mice showed a blunted/ impaired OKR compared to control mice, indicating the presence of visual deficits following a TBI.
- The Optokinetic Response is not sensitive enough behavior to detect light aversion post-TBI if it exists in mice.

Limitations

- Rod photoreceptors were oversaturated or there was no dark adaptation between light intensities.
- OKR testing may have needed to begin immediately after the TBI was administered or more time should have passed after TBI was administered to observe light aversion.
- Grating size used in OKR machine might not have been the correct size to trigger this response frequently.

Future directions

- Determine photoreceptor loss with immunohistochemistry.
- Use the spectral analysis of electroretinographic (ERG) responses to assess retinal function in TBI mice.
- Utilizing a stress assay such as the light dark box to assess whether darker or brighter light intensities are preferred by mice.
- Utilizing a pain assay will potentially explain the mechanism of photalgia in TBI patients.

References

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