

Understanding Syndrome Of The Trephined: Analyzing Balance, Coordination, And Gait After Decompressive Craniectomy In A Mouse Model Of Traumatic Brain Injury

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Background

- Traumatic brain injury (TBI) and stroke account for nearly 1 million hospitalizations annually in the U.S.³
- These patients often require decompressive craniectomy (DC), a lifesaving procedure that relieves elevated intracranial pressure.¹
- In the interval between DC and cranioplasty, patients may develop Syndrome of the Trephined.
- Syndrome of the Trephined (SoT)** = neurological dysfunction following craniectomy that improves with cranioplasty.
- Common clinical symptoms include:²
 - Motor weakness
 - Cognitive deficits
 - Language deficits
 - Altered mental status
 - Seizures
- Clinical presentation is varied, and diagnostic criteria is not well-defined.⁵
- SoT occurs in 13%-23% of patients and may still be underdiagnosed.⁴
- The underlying pathophysiology has yet to be fully elucidated.
- There is a great need to better characterize SoT.



Figure 1. A patient with SoT before and after cranioplasty. Following bone resorption of the autologous bone, this patient has sunken skin over bilateral craniectomy sites. The CT scan shows the concavity of her brain. She presents with SoT symptoms that include altered mental status, cognitive deficits, and motor deficits. After bilateral cranioplasty with alloplastic implants, her brain conforms to the normal shape of her cranium, and she shows improvement in all SoT symptoms.⁶

Aim

- To utilize a novel mouse model of TBI and DC to determine if neurological dysfunction arises solely from brain injury or if removal of skull segment contributes to it.

Hypothesis

- Lack of skull replacement will lead to increased neurologic dysfunction seen in behavioral testing.

Methods

- This experiment involved four groups of adult C57/BL6 mice.
- All mice first received a craniectomy in which a portion of the right parietal bone was removed.
- A controlled cortical impact (CCI) model was used to administer TBI.⁷
- Group 1 serves as the control group.
- Group 2 represents true SoT.

Experimental Groups:

Group 1: Immediate bone replacement (**R**)

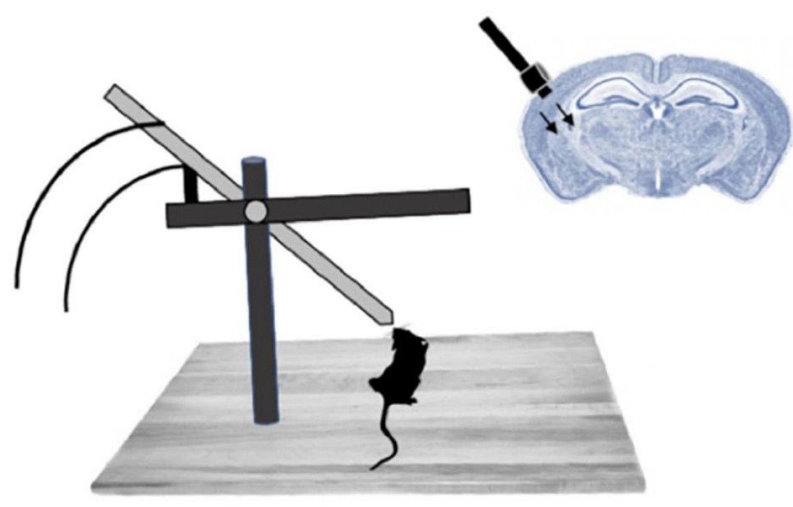
Group 2: No bone replacement (**NR**)

Group 3: TBI + immediate bone replacement (**TBI+R**)

Group 4: TBI + no bone replacement (**TBI+NR**)



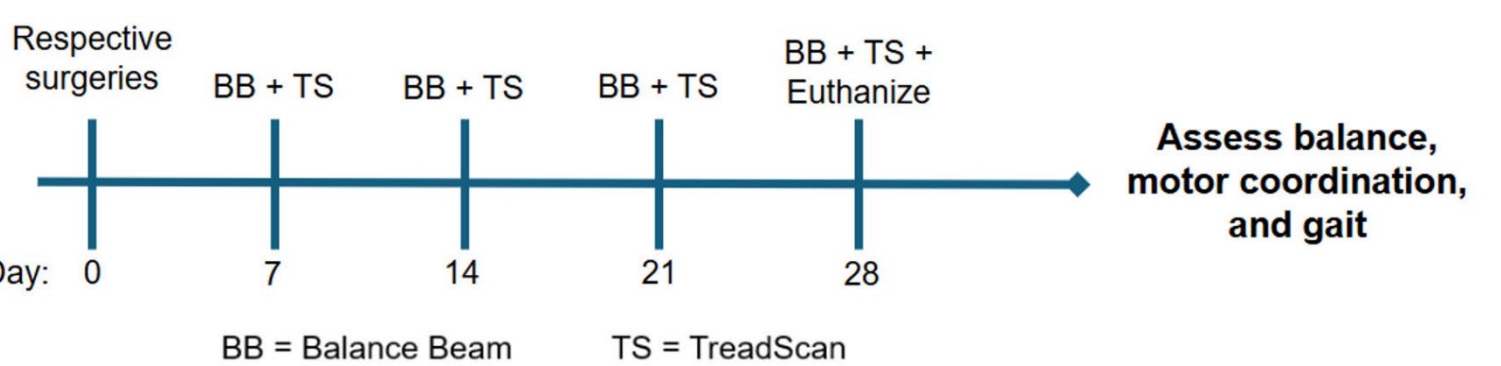
Figure 2. Surgical model of SoT. From left to right, the craniectomy site is marked on the right parietal bone, the bone flap is removed, and the bone flap is replaced.



Controlled cortical impact model

Figure 3. CCI apparatus. A cylindrical metal rod strikes the right parietal lobe to administer a TBI to the mouse.

- Neurologic function was assessed at baseline and weekly for four weeks post-surgery using Balance Beam tests and TreadScan gait analysis to evaluate balance, motor coordination, and gait.



- Number of foot slips was recorded from Balance Beam testing.
- Stance Time (ms) and Stride Length (mm) were recorded from TreadScan gait analysis testing.

Results

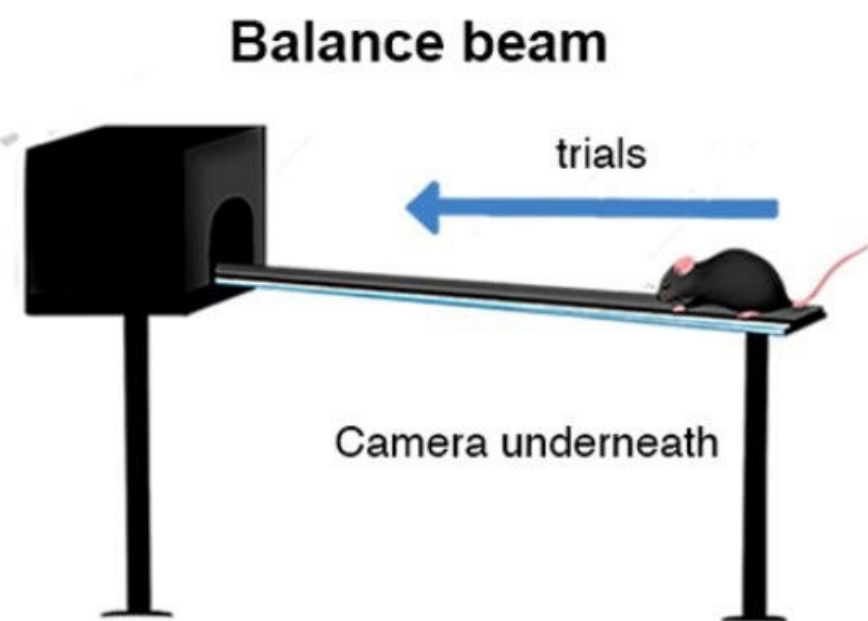
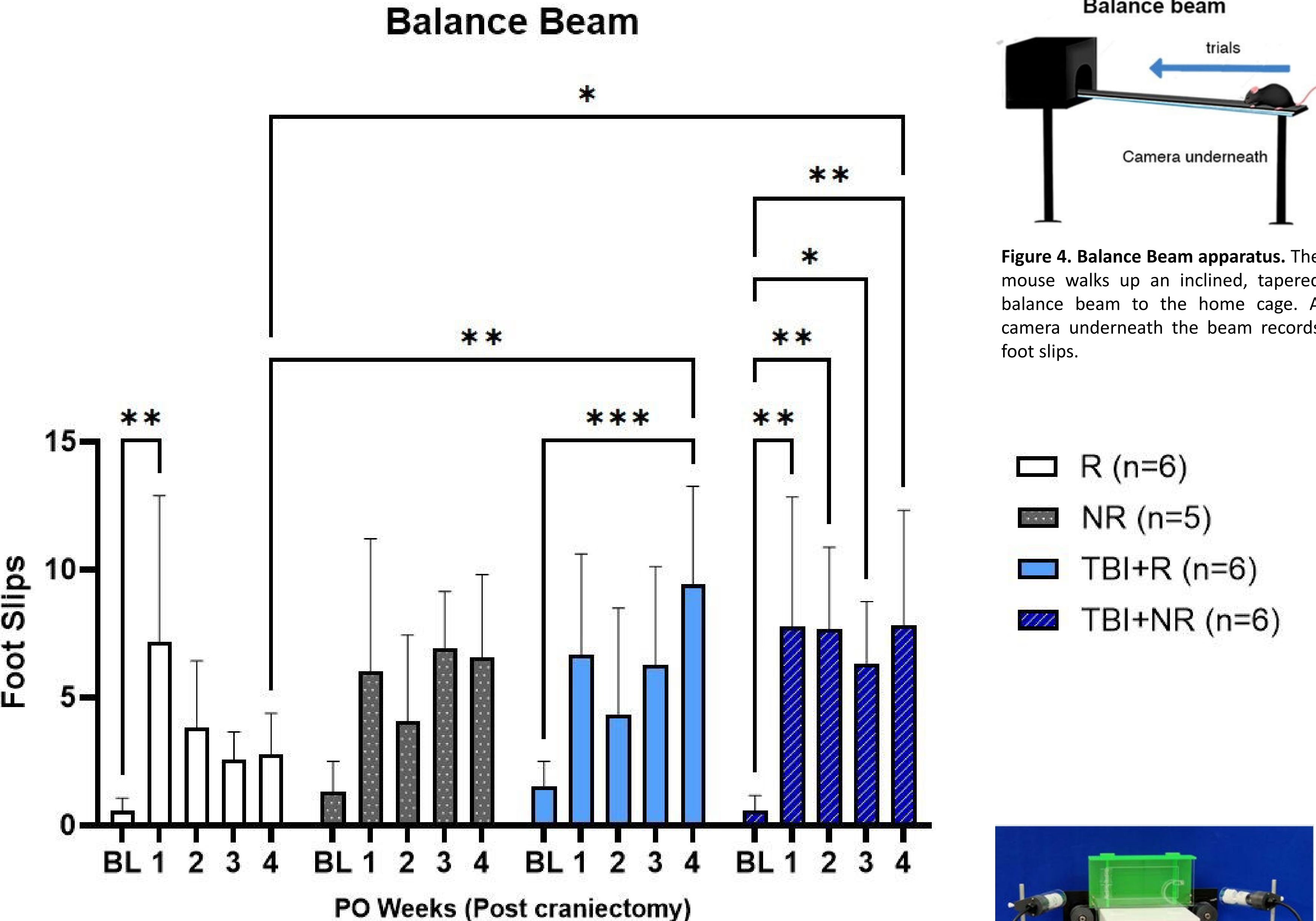
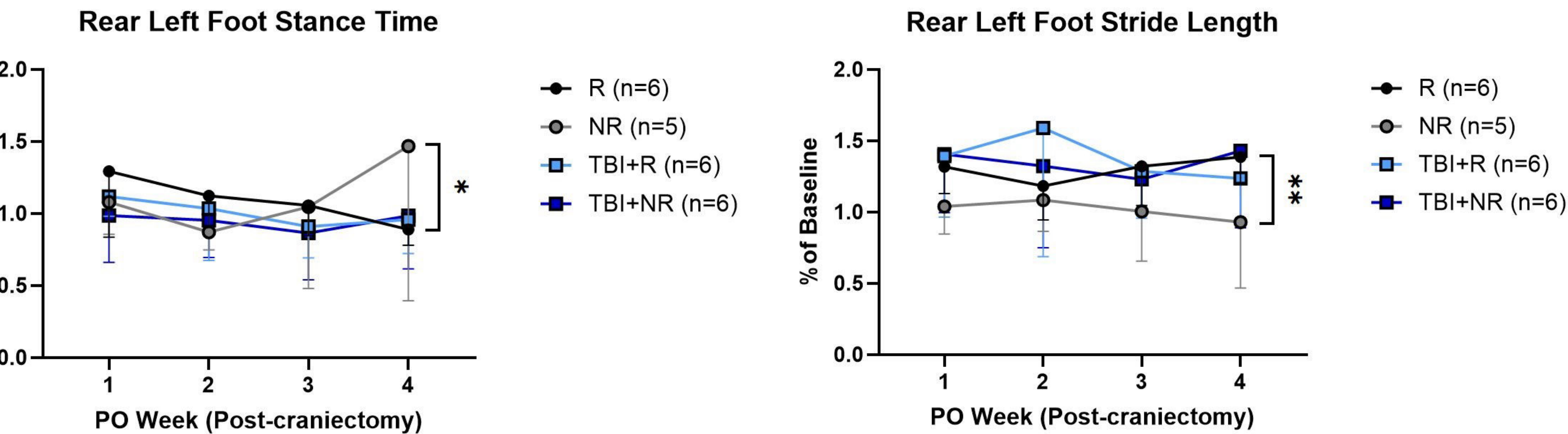


Figure 4. Balance Beam apparatus. The mouse walks up an inclined, tapered balance beam to the home cage. A camera underneath the beam records foot slips.



Figure 5. TreadScan apparatus. The mouse walks on a treadmill in a chamber illuminated by green light. A camera records data.



Discussion and Conclusion

- As expected, all mice showed an increased number of foot slips in the first PO Week after surgery.
- R mice began to show improvement in foot slips in the second PO Week.
- NR mice show significant deterioration at PO Weeks 3 and 4 that is similar to both TBI groups.
- NR mice showed significant deviation from baseline compared to R mice in stance time and stride length at PO Week 4.
- Interestingly, both TBI groups do not show this deviation.
- Together, these data show that craniectomy without bone replacement worsens fine motor coordination, balance, and possibly gait.
- Deficits from lack of bone replacement are apparent both in and out of the context of TBI.
- This preliminary data suggests that we are able to replicate findings seen in clinical populations.
- The Balance Beam appears to be an effective way to evaluate motor function in mice.
- The TreadScan may not be as sensitive to motor and gait deficits expressed in this murine model.

Future Directions

- Using this novel mouse model, we can investigate other SoT symptoms, such as cognitive deficits, altered mental status, and additional measures of motor deficits.
- These experiments could incorporate contextual fear conditioning, open field analysis, and rotarod performance testing.
- The impact of early vs. delayed cranioplasty on SoT symptoms should be further studied.
- This study could have benefited from an increased sample size and longer time points following surgery.

Citations

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Acknowledgements

The authors would like to thank Dr. Kerry-Ann Mitchell, MD, PhD for her mentorship and contributions to the field of neuroplastic surgery.

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