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VETERINARY MEDICINE

A New Rat Model of Repeat Mild Traumatic Brain Injury During Adolescence

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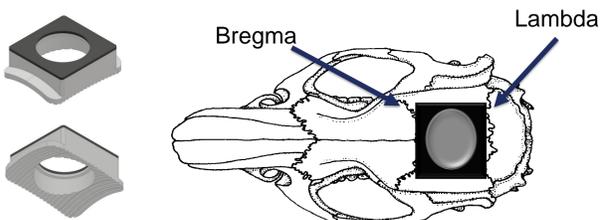


INTRODUCTION

- Contact sports are a leading cause of TBI in adolescents
- Brain injury disrupts normal development, so specific models of injuries in adolescence are needed
- Clinically, repeat TBIs are often characterized by progressive cognitive and behavioral impairment in the absence of obvious brain volume loss or motor deficits
- Mechanisms and timing of precipitating events are poorly understood
- Our model combines aspects of the Impact Acceleration and Controlled Cortical Impact (CCI) models

MODEL & METHODS

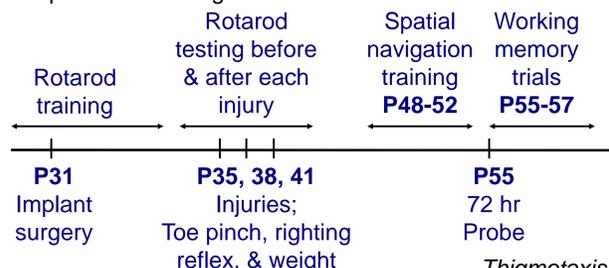
Multiple mild sports-like injuries without multiple survival surgeries



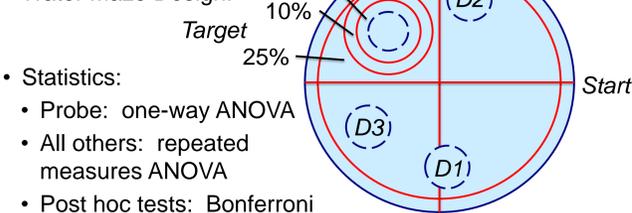
- Cap fits over metal disc (d=10 mm, h = 3 mm) and is surgically implanted for duration of experiment
- Male Sprague Dawley rats injured by striking the metal disk with the CCI device (5 m/s, 5mm depth)
 - *Sham* (n=10): 5 min isoflurane (in 2 N₂O: 1 O₂)
 - *Repeat Injury* (n=10): 5 min isoflurane + injury
 - *Single Injury* (n=7): 5 min isoflurane only on post-natal day (P) 35 & 38; isoflurane + injury on P42

Biological, motor, and cognitive effects of injury were assessed

Experimental Design:



Water Maze Design:



Statistics:

- Probe: one-way ANOVA
- All others: repeated measures ANOVA
- Post hoc tests: Bonferroni

HYPOTHESIS: Impacting a metal disc (helmet) using an electrically-driven piston will produce spatial learning deficits without skull fracture or hippocampal cell death, which can be used to model mild sports-induced TBI

Figure 1: Multiple injuries did not affect biological response or motor function

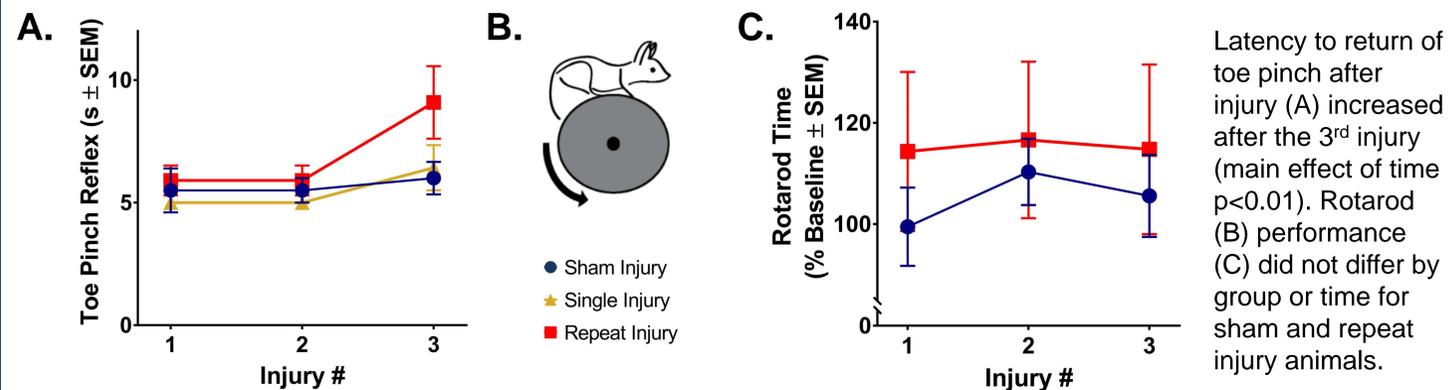


Figure 2: Multiple injuries did not affect performance on a spatial learning task

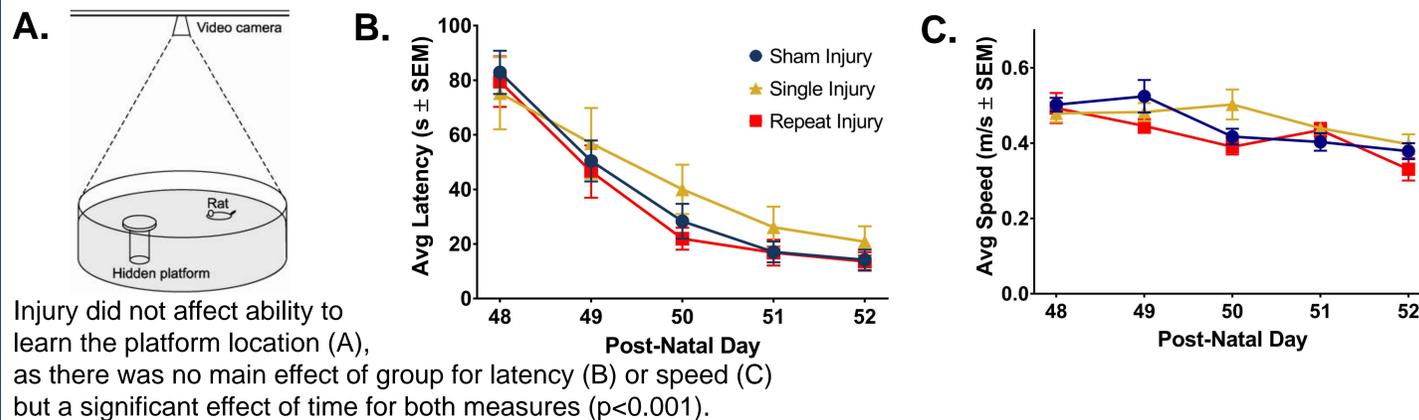
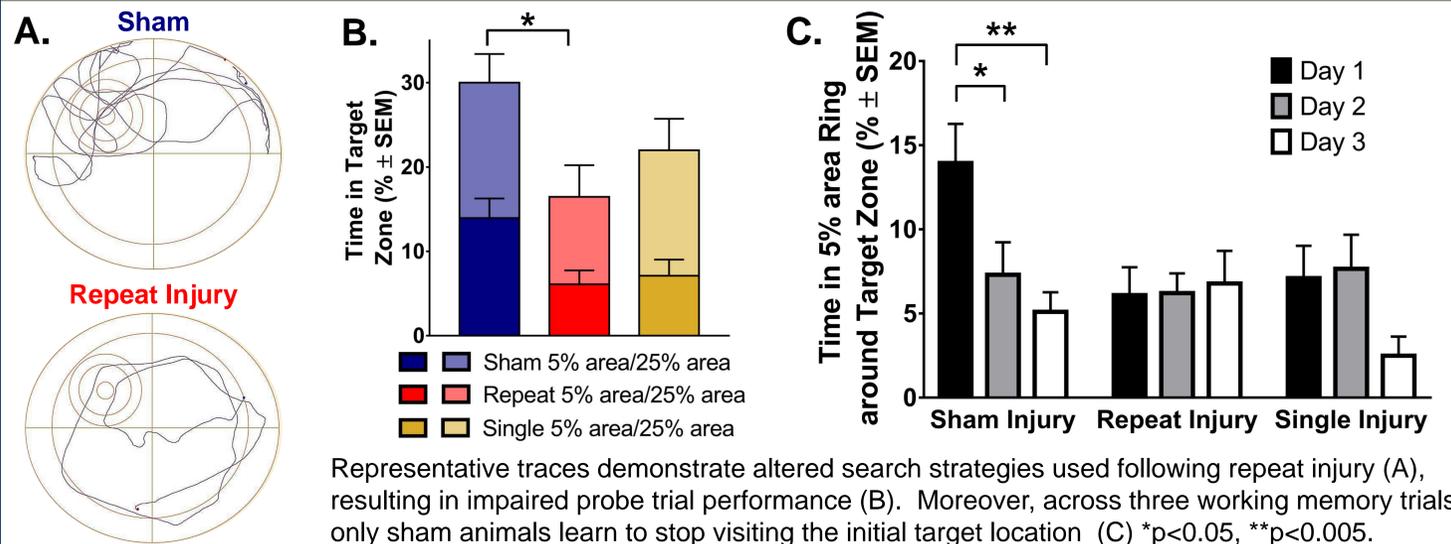


Figure 3: Repeat injury altered search strategy on water maze probe trials



CONCLUSIONS & FUTURE DIRECTIONS

Summary: Repeat injury caused cognitive deficit without motor dysfunction

- Advantages of Model:
 - Minimizes soft tissue trauma and stress on animals
 - Pre-injury anesthesia time minimized to 5 min
 - Ability to administer NSAIDs after surgery without affecting injury
- Biological effects:
 - Latency to toe pinch & righting reflexes trended towards significant increase after the third injury, suggesting a cumulative effect
 - Injury did not affect weight
- Motor effects:
 - Repeat injury did not affect Rotarod performance
 - Injury did not affect swim speed
- Cognitive effects:
 - Spatial learning did not differ during 5 days of acquisition or on the working memory task
 - Sham animals spend significantly more time searching the original target zone on probe trial but spend progressively less time searching this area over 3 days of working memory trials
 - Repeat injury animals demonstrate an alternate search strategy on probe trials

Future work: Further explore the impacts of repeat TBI and probe the anatomical changes correlated with deficits

- Assess damage to hippocampal cell populations
- Explore additional combinations of mild and moderate injuries or alter inter-injury interval
- Examine other cognitive, anxiety, and social tasks
- Adapt materials to better recreate axial rotation in sports-induced TBI
- Objective: To optimize this new model in order to test mechanisms of and therapeutics for mild sports-induced TBI

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