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; understanding the absence of obvious brain volume loss or motor deficits is 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, 5 mm 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: Rodarod testing before & after each injury, Spatial navigation training, Working memory trials
- Bregma, Lambda
- Water Maze Design: Target, Thigmotaxis
- Water Maze: 5 trials/day, 5% (466), 10% (466, 18)
- 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

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

REFERENCES & ACKNOWLEDGEMENTS