Immunosuppression Following Traumatic Brain Injury in a Rat Model

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Introduction

Severe traumatic brain injury (TBI) is a major cause of death and disability. There is a growing body of research to indicating that severe TBI patients are at acute risk of severe infection while in the intensive care unit (ICU). This increased risk of infection correlates with an acute decline in systemic immune function, sometimes referred to as immunoparalysis. There is limited understanding as to why immunoparalysis occurs following brain injury. We have developed an animal model of brain injury in rats that recapitulates this phenomenon for preclinical study.

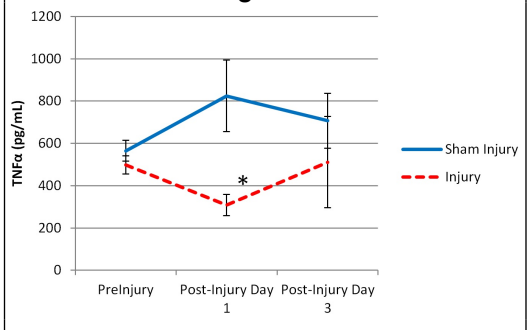
Methods

Adult Sprague-Dawley rats were used for all experiments. A moderately severe brain injury at the prefrontal cortex was induced using a controlled cortical impact model. Blood draws were performed before injury and on days 1 and 3 following injury. Immune response was determined by assessment of tumor necrosis factor alpha (TNFa) production capacity. Neurological injury from the TBI was confirmed using a Barnes maze. Gross histology of the lesion was examined using luxol fast blue and hematoxylin and eosin.

Results

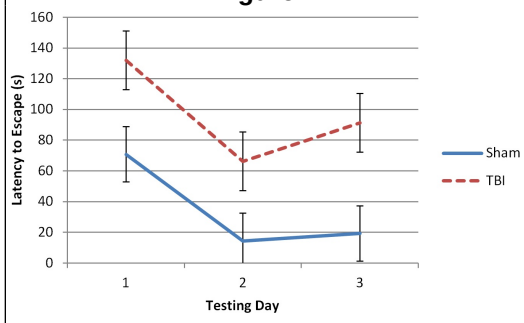
A significant, 67% decrease in TNFa production capacity following induced TBI was noted at post-injury day 1, as compared with sham-surgery animals. In the injured animals, this decrease in immune response normalized by post-injury day 3. The induced injury led to significant impairments in spatial memory and learning. The induced injury also produced a lesion cavity still notable at 4 weeks post-injury.

Figure 1



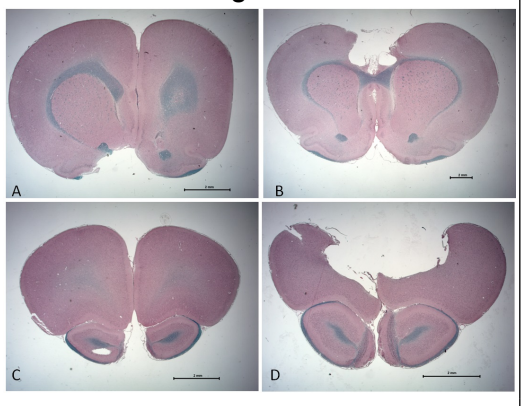
Results from the ex-vivo TNF production capacity assay both prior to injury and following injury. (n=4, *P<0.05)

Figure 2



Mean latency to escape form a Barnes Maze at post-injury days 8-10 (n=4).

Figure 3



Representative slides are shown from rat brains harvested at 4 weeks post injury from sham-injury (A, C) and TBI (B, D).

Conclusions

The data presented demonstrate that induced TBI led to a significant decline in immune function immediately following the injury. These findings mirror observations seen in TBI patients. The creation of an animal model of post-TBI immunoparalysis may allow for improved understanding of the mechanism, improved diagnostic tools for its detection, and more specific, directed therapy.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the importance of immunoparalysis following traumatic brain injury, 2) Discuss, in small groups, the possible consequences and advantages of immunoparalysis following traumatic brain injury 3) Identify possible methods for preventing/treating immunoparalysis following traumatic brain injury.