Alterations of Neurogenesis-associated Signaling Pathways in Dentate Gyrus Following Traumatic Brain Injury

Benjamin Ramser[1]; Jennifer L McGuire, PhD[2]; Laura B Ngwenya, MD, PhD[2]

[1]University of Cincinnati College of Medicine
[2]Department of Neurosurgery, University of Cincinnati College of Medicine, Cincinnati, OH

Introduction: Traumatic brain injury (TBI) is the leading cause of death and disability for people under the age of 45 years old. This complex injury process causes functional deficits through primary and secondary mechanisms. The primary injury results from physical force and can only be targeted through prevention. Secondary injury involves a cascade of events including excitatory neurotransmitter release, mitochondrial damage, changes in protein expression, and cell death. One area that is particularly vulnerable to TBI is the hippocampus, resulting in neurogenesis that is believed to hinder cognitive recovery. Currently, the differences in signaling pathways between maladaptive neurogenesis after TBI and adaptive neurogenesis, such as after exercise, is not known. This study looks at post-TBI changes in signaling pathways previously shown to play a role in neurogenesis.

Hypothesis: Neurogenesis signaling pathways in the dentate gyrus remain dysregulated 2 weeks after traumatic brain injury.

Methods: Sprague-Dawley rats were randomly assigned to one of three experimental groups: the first underwent TBI through lateral fluid percussion injury, the second were the sham group that did not undergo the injury, and the third is the running group that did not undergo the injury but were placed in a cage with a running wheel. At post-injury day 15, the dentate gyrus was dissected out. Western blot analysis was used to measure the protein concentration of phosphorylated and total AKT and GSK3β.

Results: Compared to sham, running and TBI did not have an effect on the phosphorylation to total kinase ratio of AKT or GSK3β. While it appeared that TBI increased phosphorylation of AKT and decreased phosphorylation of GSK3β relative to the running group, the effect did not reach significance.

Conclusions: Running does not have an impact on the AKT-GSK3β signaling pathway compared to sham at the time point examined. TBI does not cause a significant change in AKT or GSK3β phosphorylation compared to sham and running groups two weeks after injury. Maladaptive neurogenesis could be triggered by alterations in AKT-GSK3β signaling at different time points after injury or changes in other signaling pathways, such as through ERK and MAPK signaling.

Acknowledgements: This study was supported by a University of Cincinnati Gardner Neuroscience Institute Neuroscience Research Pilot Grant and by NIH grant T35DK060444.