Administration of Fatty Acid Emulsions to Reduce Secondary Brain Injury in Mice

Clifford Rodgers MS1, Ashish Chowdary, Ming-Mei Liu, Deborah Carlson PhD, Steven E. Wolf MD, Joseph P. Minei MD, Joshua Gatson PhD
University of Texas at Southwestern Medical Center, Department of Surgery

UT Southwestern Medical Center

Introduction:

Mild traumatic brain injuries are the most common type of injuries to the head. Seventy-five to eighty percent of all traumatic brain injuries (TBI) are considered a mild TBI, or concussions, and involve only a short interruption of mental state and consciousness. Preclinical research and clinical trials have been aimed at developing therapies to improve functional outcomes after TBI but these therapies have failed to demonstrate efficacy. Although the FDA reports no nutritional supplements for TBI therapy and/or symptom prevention, preclinical data has suggested that omega- 3 poly unsaturated fatty acid (PUFAs) treatment decreases apoptosis, inflammation, and neurodegeneration following brain trauma. In this study, we hypothesized that Smoflipid® reduces inflammation in the brain of adult mice that have suffered a mild-to-moderate brain injury. Smoflipid® is an injectable liquid emulsion solution that contains omega-3, omega-6, omega-9, and medium chain triglycerides.

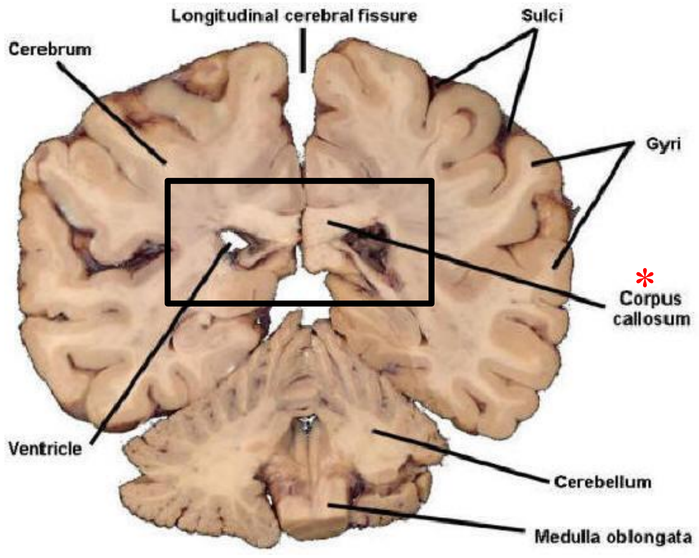


Figure 1 highlights the Corpus Callosum which is the area of interest in our study. The Corpus Callosum has a primary function of integrating motor, sensory, and cognitive performances between the cerebral cortex on one side of the brain to the same region on the other side.

Methods:

Mice were subjected to a mild-to-moderate brain injury using the controlled skull impact device (Leica microsystems) and we administered Smoflipid® intraperitoneally at day 1 and 3 after injury. At Day 14 after injury and treatment, the mouse brains were harvested, processed, and using immuno-histochemistry stained for the inflammatory marker, Iba1.

Results:

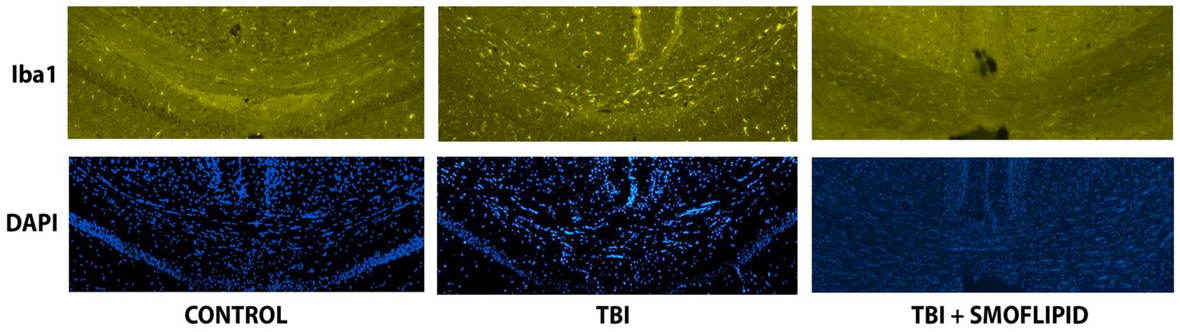
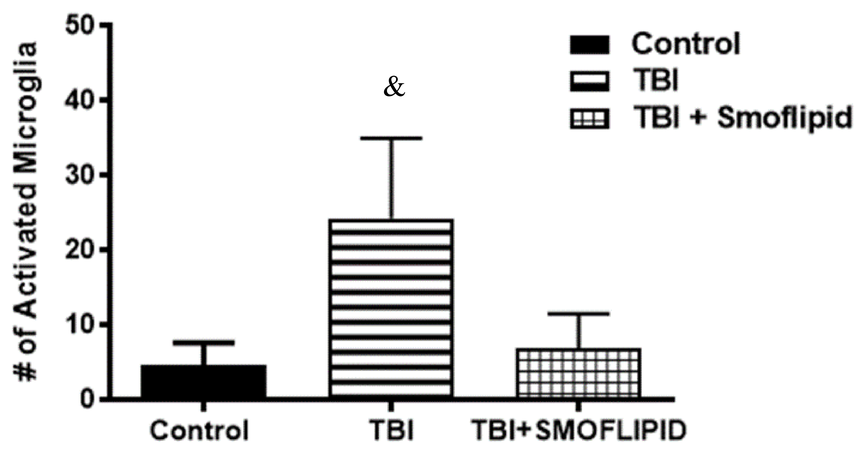


Figure 2 shows Iba1 (top row) and DAPI (bottom row) staining within the Corpus Callosum. The top row illustrates the microglial activity changes in the C.C. of mice with no TBI (left), TBI with no treatment (middle), and TBI with Smoflipid® treatment (right).



Graph 1 shows the respective microglial activity for the control, TBI, and TBI+Smoflipid groups. There was a significant elevation of activated microglia in mice that were subjected to TBI when compared to the control group. There is a reduction in activated microglia with mice subjected to TBI and treated with Smoflipid® intraperitoneally.

Results con't:

In this study, after TBI, within the Corpus Callosum (C.C.), there was a significant increase in the levels of activated microglia (Day 14, $p=0.05$) compared to the control animals. Treatment with Smoflipid® shortly after injury, resulted in a significant decrease in the number of active microglia within the C.C.

Conclusion:

Chronic activation of microglia and heightened inflammation in the Corpus Callosum after TBI, results in cognitive decline and long-term memory deficits. As a therapeutic strategy, by targeting these pro-inflammatory cells with Smoflipid®, we hypothesize that a reduction in the activity of microglia will improve neurological outcomes within the TBI population.

Future Studies:

We plan to apply more definitive clinical studies to test the efficacy of Smoflipid® at reducing secondary brain injury after TBI and possibly identify other regions of the brain that may be affected.

Acknowledgments:

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