Short Chain Fatty Acid Supplementation Improves Neurocognitive Outcomes After Traumatic Brain Injury In Mice

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ABSTRACT

Over 3 million Americans sustain a traumatic brain injury (TBI) annually with significant long-term morbidity resulting in motor, cognitive and behavioral deficits. Evolving evidence suggests that post-TBI disruption in the gut microbiome may play a role in these long-term neurocognitive outcomes. In particular, post-TBI depletion of commensal bacteria responsible for fermenting dietary fiber into short-chain fatty acids (SCFA) is an increasing area of interest. Severe TBI or sham-injury was induced in 15-week-old (n=32) male C57BL/6 mice via controlled cortical impact. The short-chain fatty acids acetate, butyrate, and propionate vs. vehicle were added to the drinking water post-injury. 45-days post-TBI or sham-injury, mice underwent neurocognitive testing with open-field testing and cued fear conditioning to assess learning, memory, and anxiety. Data analyzed using one-way ANOVA and Tukey’s multiple comparison test. TBI mice supplemented with SCFA post-injury displayed preservation of normal anxiety-like behavior than vehicle-treated TBI mice as measured by time spent in the center region of the open field (19.75 ± 6.1% time vs. 29.9 ± 4.9% time, p=0.004) (Figure 4). In addition, we observed significant preservation of associative learning and memory in SCFA treated TBI mice as compared to the vehicle-treated TBI mice as measured by cued fear conditioning (68.44s ± 12.99% time freezing vs. 29.90 ± 17.77 % time freezing, p<0.0005) (Figure 5).

INTRODUCTION

Trauma is the leading cause of death and disability in patients between the ages of 1-44 with significant long-term morbidity resulting in motor, cognitive and behavioral deficits. Evolving evidence suggests that post-TBI disruption in the gut microbiome may play a role in these long-term neurocognitive outcomes. In particular, post-TBI depletion of commensal bacteria responsible for fermenting dietary fiber into short-chain fatty acids (SCFA) is an increasing area of interest. Severe TBI or sham-injury was induced in 15-week-old (n=32) male C57BL/6 mice via controlled cortical impact. The short-chain fatty acids acetate, butyrate, and propionate vs. vehicle were added to the drinking water post-injury. 45-days post-TBI or sham-injury, mice underwent neurocognitive testing with open-field testing and cued fear conditioning to assess learning, memory, and anxiety. Data analyzed using one-way ANOVA and Tukey’s multiple comparison test. TBI mice supplemented with SCFA post-injury displayed preservation of normal anxiety-like behavior than vehicle-treated TBI mice as measured by time spent in the center region of the open field (19.75 ± 6.1% time vs. 29.9 ± 4.9% time, p=0.004) (Figure 4). In addition, we observed significant preservation of associative learning and memory in SCFA treated TBI mice as compared to the vehicle-treated TBI mice as measured by cued fear conditioning (68.44s ± 12.99% time freezing vs. 29.90 ± 17.77 % time freezing, p<0.0005) (Figure 5).

METHODS

Figure 1. Severe TBI via Murine Model

Figure 2. Murine Model Exhibit Severe TBI

RESULTS

Figure 3. Open Field

Figure 4. SCFA treated TBI Show Preservation Of Anxiety-Like

Figure 5. SCFA Treated TBI mice Show Preservation Of Connectivity Between Amygdala, Hippocampus, and Prefrontal Cortex

CONCLUSION

Dietary supplementation with short-chain fatty acids markedly improved memory, learning and anxiety measures as compared to vehicle-treated TBI post injury.

• These data suggest preservation of the connectivity between the hippocampus and prefrontal cortex in SCFA treated TBI mice.

• Vehicle-treated TBI mice showed marked disinhibition of normal anxiety-like behavior suggesting a greater loss of connectivity between the amygdala and hippocampus as compared to SCFA treated TBI mice.

• These data suggest a therapeutic benefit of SCFA supplementation after TBI.

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