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“Impact of Traumatic Brain Injury and Ethanol Exposure on Mitochondrial Bioenergetics and Behavior in the Retrosplenial Cortex of Female Rats”

Background

Traumatic brain injury (TBI), a leading cause of long-term neurological disability, demands substantial energy for recovery, a process dependent on optimal mitochondrial function. Chronic alcohol exposure is dependent on mitochondrial metabolism to mitigate the damaging effects on neural tissue. Although both TBI and alcohol are known to impair mitochondrial function in various brain regions, their individual effects on TBI recovery near the site of injury is poorly understood in females. This study aims to evaluate the impacts of TBI and sub-chronic ethanol vapor exposure on mitochondrial bioenergetics and behavior in the retrosplenial cortex (RSC), a brain region involved in working memory, with the goal of informing their combined effects.

Methods

To study the effects of post-TBI ethanol exposure on mitochondrial bioenergetics in the RSC and related behaviors, adult female Wistar rats were assigned (n=6-12/group) to Sham, Sham + Ethanol (EtOH), TBI, or TBI+EtOH groups. Following craniotomies and four days post-TBI or Sham-procedure, EtOH animals were placed into alcohol vapor chambers targeting ~200 mg/dl for ten days. Open field and spontaneous alternation testing were conducted six hours after the final EtOH exposure (during early withdrawal). RSC tissue was collected 24 hours later for mitochondrial respiration analysis.

Results

TBI induced up to a ~5% loss in body weight ($p < 0.05$) during the first six days post-injury. EtOH induced a decrease in body weight ($p < 0.05$) after blood alcohol levels reached 200 mg/dL (spanning from day 8 to 12 post-TBI), with a peak loss of ~4%. The TBI+EtOH group exhibited sustained weight loss ($p < 0.05$) throughout the first 12 days, reaching a peak decline of ~6% before beginning to recover. Mitochondrial respiration analysis of RSC showed a ~38% reduction in the EtOH group ($p < 0.01$) and ~33% reduction in the TBI group ($p < 0.05$) in basal respiration in comparison to control. Maximal respiration was decreased by ~32% in the TBI group ($p < 0.001$) and by ~33% in the EtOH group ($p < 0.001$). Furthermore, the basal and maximal respiration from the TBI+EtOH group did not show significant differences to either TBI or EtOH groups. Non-mitochondrial oxygen consumption was elevated by ~39% in the TBI group ($p = 0.056$) and no change with EtOH and TBI+EtOH group.

Conclusion

This study found significant transient reductions in body weight resulting from EtOH and/or TBI insult. A reduction in basal and maximal respiration with both TBI and EtOH, without additive effects when combined, suggests that these insults act through overlapping mechanisms that reveal emerging bioenergetic vulnerabilities. Furthermore, the increase in non-mitochondrial oxygen consumption with TBI suggests a compensatory shift in oxygen utilization. Moving forward, sample size will be increased to strengthen the robustness of these findings.