Aged Mice Demonstrate Preserved Learning And Memory After Traumatic Brain Injury Compared To Young Mice

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ABSTRACT

Over 3 million Americans sustain a traumatic brain injury (TBI) annually. Age-related differences in brain physiology and comorbidities may lead to divergent outcomes in aged versus young patients. However, few studies have addressed age as an independent variable. We hypothesized that aged mice would have greater deficits in learning, memory, and anxiety behavior after TBI or sham injury was induced in 14-week-old (n=21) and 80-week-old (n=24) male C57BL/6 mice via controlled cortical impact. 30-days post-TBI mice underwent open field testing and cued fear conditioning to assess learning, memory, and anxiety. Data was analyzed using one-way ANOVA and Sidak’s multiple comparison test. TBI of sham injury was induced in 14-week-old (n=21) and 80-week-old (n=24) male C57BL/6 mice via controlled cortical impact. 30-days post-TBI mice underwent zero-maze testing and cued fear conditioning to assess learning, memory and anxiety. Young TBI spent more time in the open regions of the zero-maze demonstrating marked disinhibition of normal anxiety-like behavior (Figure 4). Aged TBI mice demonstrated preserved associative learning and memory as compared to young TBI mice after cued fear conditioning. Additionally there was a difference between Aged Sham and Young Sham (Figure 5).

METHODS

Figure 1. Severe TBI via Murine Model

Figure 2. Murine Model Exhibit Severe TBI

Figure 3. Histology and MRI Confirm Severe TBI

RESULTS

Contrary to our hypothesis, aged mice had attenuated deficits in learning, memory, anxiety measures as compared to young mice after TBI:

• These data suggest relative preserved connectivity between the hippocampus and prefrontal cortex in aged mice after TBI.
• Additionally, young TBI mice showed marked disinhibition of normal anxiety-like behavior suggesting a greater loss of connectivity between the amygdala and hippocampus compared to aged TBI mice.
• These data demonstrate different pathophysiology in the aged vs. young brain after TBI suggesting that different treatment and rehabilitation strategies are needed for aged and young TBI patients.

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INTRODUCTION

Trauma is the leading cause of death and disability in patients between the ages of 1-44 with TBI’s contributing to a nearly a third of them. Presently, approximately 2% of the U.S. population are afflicted with disabilities and behavior deficits as a result of a TBI. Despite promising preclinical data, clinical trials have failed to produce effective therapies for this highly morbid injury process. If fact, most clinical trials of TBI have included patients ranging in age from adolescence (~15yrs) to more advanced age (>65yrs). This despite epidemiological data which suggest that aged TBI patients have worse outcomes as compared to young TBI patients.

RESEARCH OBJECTIVES

Our research objective was to assess age as an independent variable in neurocognitive tests of learning, memory, and anxiety behavior after TBI. To further these Aims, We hypothesized that aged mice would have greater deficits in learning, memory, and anxiety behavior after TBI.