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MINO plus NAC Alleviates Memory Deficits and Diminishes Neuroinflammation in Female Mouse Closed Head Injury Model

Traumatic brain injury (TBI) is a major cause of disability. Despite promising results in rodent models, no treatment has proven to be effective in human trials. One potential reason for failed trials is insufficient preclinical testing in females. Our laboratory demonstrated that combining two FDA-approved drugs Minocycline and N-acetylcysteine (MINO plus NAC) prevents memory deficits, diminishes neuroinflammation, and prevents neuronal and glial loss in a mouse close head injury (CHI) model using male mice. This study examined the efficacy of MINO plus NAC treatment in female mice. Female C57/BI6 mice (16-18 weeks) received CHI or sham-CHI treatment. Injured animals were divided into two groups and were treated with either MINO plus NAC or saline starting 12 hours after injury, every 24 hours for three days. At 10 days post-injury animals were tested on Barnes Maze and perfused at 14 days post-injury. MINO plus NAC treatment started 12 hours after CHI improved the performance of female mice on the Barnes Maze. Brains were sectioned and immunostained for the marker of astrocyte activation, glial fibrillary acidic protein (GFAP). CHI produced deficits in maze acquisition and retention were similar to what was found in the male model. Injury resulted in astrocytes activation in ipsilateral thalamus and additional brain areas are currently being assessed to determine their activation. Treatment with MINO plus NAC reduced activation in the ipsilateral thalamus. This data suggest that the CHI model produces deficits in females that are similar to males. Treatment with MINO plus NAC resulted in improved performance in memory tasks and diminished astrocyte activations.