Short- and Long-Term Neuropathology associated with Repetitive Closed-Head Impact Model of Engineered Rotational Acceleration (CHIMERA) in Mice

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Repetitive mild traumatic brain injury (rmTBI) is a significant brain health issue in public and in military personnel. To study the pathophysiological mechanism of rmTBI, we evaluated short- and long-term neurodegenerative and glial responses in mouse brain following repetitive close-head impact model of engineered rotational acceleration (rCHIMERA). The mice were exposed rCHIMERA and the brains were analyzeat 2-weeks, 4-weeks and 1-year post-rCHIMERA. We observe transient neuroinflammation (increased IBA1 (microglia) and GFAP (astrocytes) staining) in multiple brain regions at 2- and/or 4-weeks but not at 1-year post-TBI. Axonal neurodegeneration (FD-NeuroSilver reaction) was transient in most brain areas. Significantly, neurodegeneration and neuroinflammation in the Optic tract (OT) and the corresponding projection regions show chronic increase that persists even at 1-year post-rCHIMERA. Finally, we observe that monoaminergic (MAergic) unmyelinated axons that are involved in neuropsychiatric function (TH+: Noradrenergic, SERT+:5-HT) were reduced in the S1 barrel cortex at 2- and 4-weeks post-rCHIMERA. Significantly, treatment with a metabolically stable GSH analog was able to completely prevent loss of MAergic afferents at 4-week post rCHIMERA. However, the neurodegenerative changes seen in OT was not reduced by GSH treatment, indicating that GSH treatment may be effective in preventing neuropsychiatric impact of rmTBI. In conclusion, these data proposes that the overall impact of the rCHIMERA pose a reasonable and enduring neuropathologic outcome of microgliosis, astrogliosis and white matter degeneration which are important hallmarks of the pathophysiologic mechanism of rCHIMERA.

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