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CHRONIC IMPAIRMENT OF CEREBRAL BLOOD FLOW IN A MOUSE MODEL OF REPETITIVE MILD TRAUMATIC BRAIN INJURY

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Repeated exposure to mild traumatic brain injury (mTBI), as seen in contact sports injuries, is known to predispose individuals to development of neurodegenerative diseases such as Alzheimers Disease and Chronic Traumatic Encephalopathy (CTE). CTE is characterized by deposition and hyper-phosphorylation of the microtubule-associated protein tau throughout the brain. In addition to aberrant proteinopathy, neurodegenerative diseases are often associated with cerebrovascular abnormalities, including changes in cerebral blood flow (CBF), and loss of Blood Brain Barrier (BBB) integrity. Owing to the prevalence of mTBI, there is an urgent requirement for animal models recapitulating the pathological hallmarks, cognitive deficits, and cerebrovascular components of neurodegeneration following repetitive mild head trauma. We used heterozygous transgenic hTau mice expressing all 6 isoforms of human tau on a null murine tau background, allowing for a clinically relevant investigation of the effects of repetitive mTBI (r-mTBI) on cerebrovascular mechanics in the presence of human tau. The closed-head mTBI was administered to mice under isofluorane anesthetic using a 5mm blunt metal impactor tip at a velocity of 5m/s and a strike depth of 1mm, positioned midway to the sagittal suture. We administered 2 hits every week for 3 months to replicate the incidence of mTBI that can occur over the course of a career in contact sports. We measured CBF in both hTau and wild-type mice 3 months and 7 months post-injury, respectively, using laser Doppler imaging. We observed a significant decrease in CBF in wild-type mice (10.66% ± 1.44% compared to sham) and hTau mice (8.92% ± 1.39% compared to sham) This effect of r-mTBI on CBF may provide rationale for the link between head trauma and the development of neurodegenerative disorders like CTE. We will continue to evaluate the impact of r-mTBI on the cerebrovasculature by assessing BBB integrity and examining specific vascular markers at various time-points post-injury in upcoming studies.

Keywords: Animal Models, Cerebral Blood Flow, Laser Doppler Imaging, hTau Mice, Closed-Head Injury