Observing changes in cerebral blood flow and hippocampal metabolites by magnetic resonance after a closed head traumatic brain injury in mice

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Background: Traumatic brain injury (TBI) and its associated morbidity are a major public health issues with an unmet need for therapeutic interventions that alter pathology progression and improve longer-term neurologic outcomes. Multimodal magnetic resonance imaging (MRI) following a TBI can be used clinically and preclinically as prognosticators of neurological dysfunction.

Purpose: The purpose of this study is to determine changes in cerebral blood flow (CBF) and hippocampal metabolites following closed head injury (CHI) in mic; a diffuse model of traumatic brain injury (TBI). Furthermore, we seek to determine if these changes occur in the subacute or chronic phase after injury.

Methods: C57/B6 mice were subjected to midline sagittal scalp incision followed by a CHI using a stereotactically guided electromagnetic impactor device. Sham-injured mice underwent identical surgical procedures as the trauma group, but no impact was delivered. Both groups of mice were scanned by 7T magnet 3 days after injury for the follow MRI sequences: arterial spin labeling (ASL) measuring cerebral blood flow and (1)H-magnetic resonance spectroscopy (MRS) to measure hippocampal metabolites. Another cohort was injured and scanned at 28 days following the CHI for the same parameters as the three day scans.

Results: Our data indicate that 3 and 28 days after CHI significantly decreased hippocampal metabolites such as N-acetyl-aspartate (NAA +NAAG), total choline (Cho), and creatine (Cr), metabolites important for maintaining neuronal integrity and brain bioenergetics. Cerebral blood flow was analyzed for specific regions of interest (ROIs): cortex proximal to injury, cortex adjacent to injury, and the hippocampus. Changes in cerebral blood flow were observed, the cortex proximal to injury and the hippocampus decreased 3 days after injury while the cortex adjacent to injury slightly increased relative to sham, however the changes did not reach significance. By 28 days post CHI, both cortical regions increased in CBF compared to sham.

Conclusions: This study provides further insight in the multimodal MRI predictors in a mild preclinical model, which could be used as a translation endpoint in preclinical and clinical studies.