

2023 Annual Research Day – Oral session  
April 19<sup>th</sup>, 2023, 2:00 p.m. – 4:30 p.m., PHAB 2A

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**Heterogeneity of chronic gray matter atrophy and spatial navigation following closed head injury**

Traumatic brain injury (TBI) is characterized by heterogeneity in pathophysiology and recovery outcomes. The mechanisms underlying this heterogeneity are poorly understood. Atrophy after moderate to severe TBI occurs early after injury or is delayed and progressive (Havlicek et al. 2023). Gray and white matter regions proximal to the injury site undergo early atrophy, with delayed atrophy in distal white matter regions. In a closed head injury (CHI) mouse model of TBI, T2 MRI reveals an early gray matter atrophy in ipsilesional cortex, thalamus, and hippocampus occurring within 14- days post injury (DPI). Cortical and thalamic atrophy is unchanged at 180 DPI. In contrast, the extent of ipsilesional hippocampal atrophy at 180DPI can be split into two groups (greater vs. less atrophy at 180DPI, N=3, N=4, respectively,  $p=0.05$ ). Both the dorsal and ventral hippocampus contributes to ipsilesional atrophy. Barnes maze assesses spatial learning and memory and is highly sensitive to hippocampal lesions. Injured mice at 180 DPI can also be divided into good or poor learners based upon Barnes maze acquisition and retention. Thus, the chronic CHI model may provide a unique ability to study the inherent heterogeneity of injured mice on Barnes maze and relate it to hippocampal atrophy. Heterogeneity in hippocampal atrophy and cognitive decline provide a potential link between Alzheimer's Disease and the TBI pathophysiology.