Exploring different pathological biomarkers in the grey and white matter of a newly developed model of chronic repetitive concussive head injury.

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Accumulation of repetitive concussive head injury experienced over the careers of professional athletes in sports, such as, boxing and American football is a major risk factor for the development of neurodegenerative diseases in later life.
We have developed a new mouse model paradigm to explore the risk of repetitive concussive head injury over a prolonged period of time, and the age-associated post-injury factor on neuropathological outcome.
Briefly this new closed head injury model involves delivering two concussive head injuries on a weekly basis, with a minimum inter-injury interval of 48 hours, repeated over 3 to 4 months. Animals were euthanized between 2 to 3 months post last injury.
To characterize and validate our model we have chosen to explore a host of relevant pathological markers. These markers include: different tau species, neurofilament H (NFL-H), α-synuclein, TAR-DNA-binding protein 43 (TDP-43), neuroglial markers (GFAP, IBA-1, CD45, vimentin), inflammatory cytokines (IL-1β, TNFα, IL-6, 1L-4, 1L-10), axonal markers (MBP, APP, Luxol fast blue, silver staining) and lipid species. We correlate these pathological and biochemical profiles with neurobehavioral outcome in tests that examine sensorimotor performance (open field), anxiety (elevated plus maze), social interaction/memory (3-chamber test) and cerebral blood flow (laser Doppler imager). Our data thus far shows a significant dramatic increase in neuroglial markers in injured animals compared with shams. Axonal integrity was significantly altered in injured animals at chronic timepoints post-injury. No significant changes were observed in α-synuclein or TDP-43. A reduction in total tau (tau46) levels was observed in correlation with an apparent increase in tau oligomer level (TOC-1). Other biochemical and behavioral analyses are currently ongoing in this model.

Key words: concussion, animal models, cytoskeletal proteins, inflammation, and axonal injury

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