Morphological and immunohistochemical characteristics of optic nerve damage post repeated traumatic brain injury

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Background: Recent studies from our group demonstrated profound deleterious effects on the optic nerve and retina from a novel, closed-head injury mouse model at 10-13 weeks post repeated mild traumatic brain injury (r-mTBI) which were accompanied by changes in visual function (J Neuropathol Exp Neurol. 2014 73:345-61). As an extension of these findings, the current work was designed to explore the effects of r-mTBI on optic nerve morphology and immunohistochemistry at earlier time points.

Methods: Adult male C57BL/6 mice (10-12 weeks old) were subjected to either r-mTBI or repetitive sham, according to an established protocol. Mice were sacrificed and optic nerves extracted and processed for paraffin embedding at 24 hours, 3 days, 7 days and 3 weeks post injury. Cellularity of the optic nerve and myelination was estimated after staining with H&E and Luxol Fast Blue(LFB). Optic nerves from naïve mice (n = 6; 6-9 month old C57BL/6 retired breeders) served as an additional control. Additionally, Immunohistochemistry staining for S100 calcium binding protein B (S100B), ionized calcium-binding adapter molecule 1 (Iba1) and CP13 antibody against pS202/T205, an early tau pathology marker was carried out also.

Results: Regions of local demyelination were observed in the optic nerves from the r-mTBI group as early as 24 hours after the last injury and at all time points afterwards. This was paralleled with increased cellularity in the r-mTBI optic nerves, an increase ranging from 59% (compared to naïve mice) at 24 hours to 38% at 3 weeks ($p<0.01$). S100 immunoreactivity remained negative, while both Iba-1 and CP13 showed increased levels in the form of either enhanced cell body staining or diffuse immunoreactivity in r-mTBI optic nerves. Curiously, the region of cavernous degeneration in the distal part of the nerve remained free of CP13 staining.

Conclusion: Increased immunoreactivity and increased cellularity was observed in optic nerve tissue after r-mTBI at 24 hours to 3 weeks post injury, indicative of an ongoing inflammatory and neurodegenerative process. This confirms the validity and usefulness of our model as a platform to further characterize the neurodegeneration associated with r-mTBI and test treatment approaches.