Short Term Mild Traumatic Brain Injury Mechanisms Characterized in an In Vivo Göttingen Minipig Model

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Abstract

Traumatic brain injury (TBI) is a recurring problem with an estimated 1.7 million occurrences annually in the United States, accounting for 30.5% of all injury-related deaths[1]. This study seeks to answer many of the unknowns surrounding mild TBI regarding the mechanisms and pathogenesis involved over 24 hours by using magnetic resonance spectroscopy (MRS) and immunohistochemistry (IHC).

A repeatable rotational injury device was used to induce mild TBI in Göttingen minipigs. The minipigs undergo baseline MR scans (7T Bruker) prior to injury, immediately post-injury, and twenty-four hours post injury, at which point the brains are perfused and harvested for IHC. MRS quantifies metabolites in a 216 mm^3 voxel placed in the genu of the corpus callosum. Metabolites of interest include glutamate (Glu), N-acetylaspartate (NAA), N-acetylaspartate (NAAG), choline, and myo-inositol.

IHC was performed on the genu with five antibodies; β amyloid precursor protein (βAPP), light neurofilament, heavy neurofilament, glial fibrillary acid protein (GFAP), and caspase-3. ImageJ was used to calculate integrated density for comparison between groups.

Two 24 hour sham control and eight 24 hour rotational injury animals have been tested. Three animals have been dropped from an angle of 15° and 25°, one from 35° and one from 40°.
Significant increases were found in NAA and Glu between all baseline and 24 hour post injury concentrations ($p<0.05$). NAAG decreases after injury, but was not significant ($p=0.1$). IHC identified a significant increase in light neurofilament ($p<0.05$) build-up between sham and injury animals ($p<0.05$). IHC analysis is currently underway to look at heavy neurofilament, GFAP, and caspase-3. One thing to note is that negligible βAPP staining occurred for all animals.

In conclusion, there are significant differences that can be seen using MRS and IHC within 24 hours. Once IHC analysis is completed, the outcomes will be correlated with the MRS results. This will facilitate interval MRS scanning during a subsequent longitudinal study of the time course development of mTBI.

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