Longitudinal 1H MRS and DTI in rodent fluid percussion brain injury model to study cerebral metabolism, brain morphology and cognitive deficits

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INTRODUCTION: Traumatic Brain Injury (TBI) can cause lasting neuropsychological damage and impair the day-to-day functionality for survivors. In this study, we have investigated the changes in brain morphology and cognitive function affected by fluid percussion injury in rodent models with Diffusion Tensor Imaging (DTI) and Magnetic Resonance Spectroscopy (MRS). The apparent diffusion coefficient (ADC), obtained from DTI, is sensitive to cell walls and bundles of nerve fibres. The destruction of barriers in injured site can be monitored by increased ADC. In this study we have assessed the ADC changes in white matter below the TBI site. MRS provides information on the changes in tissue biochemistry and metabolism at the injured site. Cognitive assessment was also carried out and correlated with changes in DTI and MRS measurements.

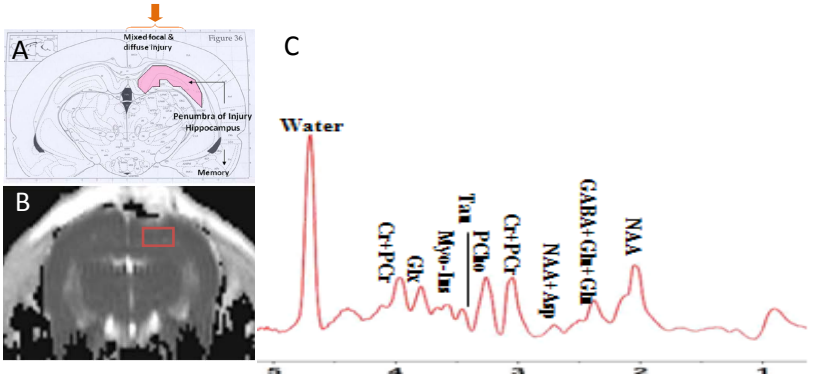

Figure 1. A) Schematic of Fluid Percussion injury administered midway between bregma and lambda and 2mm lateral to midline, arrow indicates site of injury B) DTI - ADC image, red box indicates MRS data voxel position (C) ^{1}H MRS Spectrum

METHODS: Adult male Sprague Dawley rats (n=5) were subjected to fluid percussion injury (64.04 ± 1.5psi) (Figure 1A) [1]. Imaging and cognitive assessment were performed before injury and on day 1, 3 and 7 after injury. DTI images were acquired on the rat brain in the transverse direction TR/TE=8000/50, b-value=1000, directions=20, averages=4. Image maps of ADC, fractional anisotropy and colour maps were computed and quantified using DTI Studio [2] (Figure 1B). The PRESS sequence was utilized to acquire MRS data using a voxel size of 3.0 x 2.0x 3.0 mm^3 predominantly from the cortex and corpus callosum (Figure 1C), TR/TE of 5s/13ms, and total acquisition time of 11 minutes. Results were quantified using LC Model [3]. Animals were tested on the Rotarod (0 – 24rpm in 60s) to assess for motor skills.

RESULTS: DTI observed longitudinally from baseline (before injury) to Day 1, 3 and 7 after injury shows the ADC values rise significantly after injury on Day 1 suggesting a disruption in the tissue as a result of the injury but fall back closer to baseline values by Day 7 suggesting significant changes in tissue morphology for this duration (Figure 2A). Data from MRS techniques show that the NAA/Cr ratio, an important neuronal degeneration marker, mirrors the ADC changes in the opposite direction, where the NAA/Cr ratio falls immediately after injury but recovers towards Day 7 after injury (Figure 2B). In the rotarod task, injured animals were impaired in their balance and coordination immediately after injury on Day 1 but showed progressive improvement after injury by Day 7.

Timeline	ADC (mm^2/s)	NAA/Cr (Ratio)
Baseline	7.22E-04	1.045
Day1	1.05E-03	0.486
Day3	9.71E-04	0.715
Day7	7.02E-04	0.825

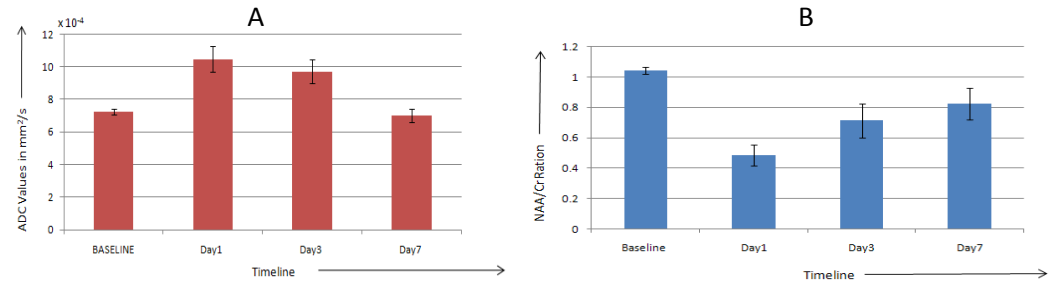

Figure 2. Data before injury (baseline) and after injury on Day 1, 3 and 7 (A) ADC values and (B) NAA/Cr values for corpus callosum below injury site

CONCLUSIONS: The current study demonstrates good correlation in results obtained by DTI and ^{1}H MRS to track white matter changes in the traumatic brain injury model in rodents. Results show an increase in ADC values immediately post injury in agreement with earlier work [4] and further show a gradual near normalization of these values over time. Corresponding MRS results also show a decrease in NAA/Cr ratio immediately post injury and trend towards earlier baseline ratio after a few days. These findings could indicate a reorganization effect taking place in the brain after being disrupted by the injury. Cognitive tests also show an improvement in test results a few days after injury, mirroring the trend of near recovery to baseline demonstrated by ADC and NAA/Cr values over the same timeframe. This suggests that regional cerebral changes in ADC and NAA/Cr values may serve as a possible prognostic and diagnostic marker for cognitive performance after TBI.

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