

Tissue outcome in areas surrounding the impact site in traumatic brain injury

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Target Audience Researchers in traumatic brain injury.

Purpose We previously reported severe and heterogeneous perfusion disruptions beyond the impacted area following mild TBI and its spatiotemporal profiles are time dependent. However, it is unclear how such hemodynamic disruption affect tissue outcome. It is possible that chronic perfusion deficits could delay cell death, leading to progressive ADC, fractional anisotropy and T2 degradation and functional deficits as often observed clinically. The goal of this study was to systematically evaluate the effects of perfusion disruptions on ADC, T2 and FA by analyzing a series of ROIs lateral to the impacted area.

Methods Male SD rats (250-350g, n=12) underwent mild TBI induced over the left forelimb somatosensory cortex through a cranial window using a Ø3mm tip (5.0m/s, 250µs dwell time, 1mm depth) (Watts, L Neurotrauma). Multislice T2, ADC, CBF MRI at 7T was acquired 1 and 3 hrs, 1, 2, 7 and 14 days after TBI under 1.5% isoflurane. The spatial resolution was 267x267x1000microns. Images were co-registered. T2, ADC and fractional anisotropy (FA) were tabulated for the lesion ROI (#1), and ROI #2-5 lateral to the impact region (Figure 1). Normalization was made against homologous regions in the contralesional hemisphere.

Results: Data from ROIs #3-5 were similar in pattern and thus only data from ROI#3 are reported.

Figure 2 shows normalized CBF, ADC, T2 and FA in the defined ROIs adjacent to the impact site. For the lesion ROI #1, CBF dropped to 20% of normal 1-3 hrs after TBI, increased to 140% of normal on day 2 (hyperperfusion), and returned toward normal on day 7 and 14. For ROI #2, CBF dropped to 60% of normal 1-3 hrs after TBI, remained depressed on day 2, and returned toward normal on day 7 and 14. For ROI #3, CBF was mostly invariant across time. Only the lesion ROI showed ADC (increase), T2 (increase), and FA (decrease) changes at 1-3 hrs and 2 days after TBI. All of these parameters return to normal on day 14.

Discussion and Conclusion: The major findings are, for FA, ADC and T2 to change, CBF had to be reduced to 20% of normal for a substantial duration in our mild TBI model. No changes in these MRI parameters were detected when CBF dropped to 60% of normal up to 14 days post TBI. In addition, CBF, FA, ADC and T2 values all recovered by day 14. These MRI findings are in marked contrast to ischemic brain injury in several aspects. First, in TBI, hyperperfusion was reversible, T2 and ADC paralleled each other, suggesting vasogenic edema is the key contributor. ADC, T2 and FA changes were mostly reversible in our model of mild TBI. In ischemic stroke, hyperperfusion and T2 abnormality are almost always associated with poor outcomes.

Normalization with respect to the homologous contralesional ROI has a drawback in that contralesional values could be affected by TBI. For the parameters measured, we did not notice any apparent differences between the homologous contralesional ROIs and those of normal animals we imaged in our previous studies, nor did we find any apparent time dependent changes in the homologous contralesional ROI. In conclusion, this mild TBI model multiparametric MRI offers a means to probe tissue fates at graded CBF reduction. The lessons learned will likely provide useful, clinically relevant information for further characterizing mild TBI injury and other brain injuries in both animal models and humans.

REFERENCES [1] Shen Q, et al., J Cereb Blood Flow Metab, 2011; 31, 2076. [2] Shen Q, et. al., Severe Perfusion Disruption beyond the Impact Area in Hyperacute, Acute and Chronic TBI; ISMRM Submitted Abstract 2014.

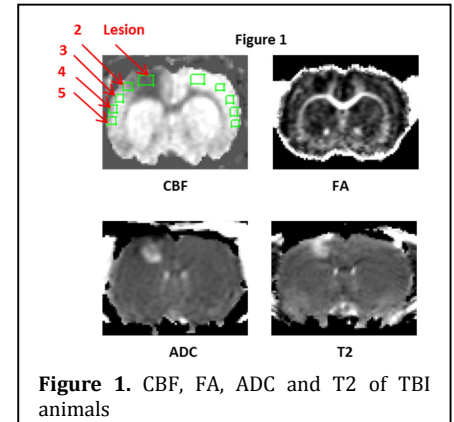


Figure 1. CBF, FA, ADC and T2 of TBI animals

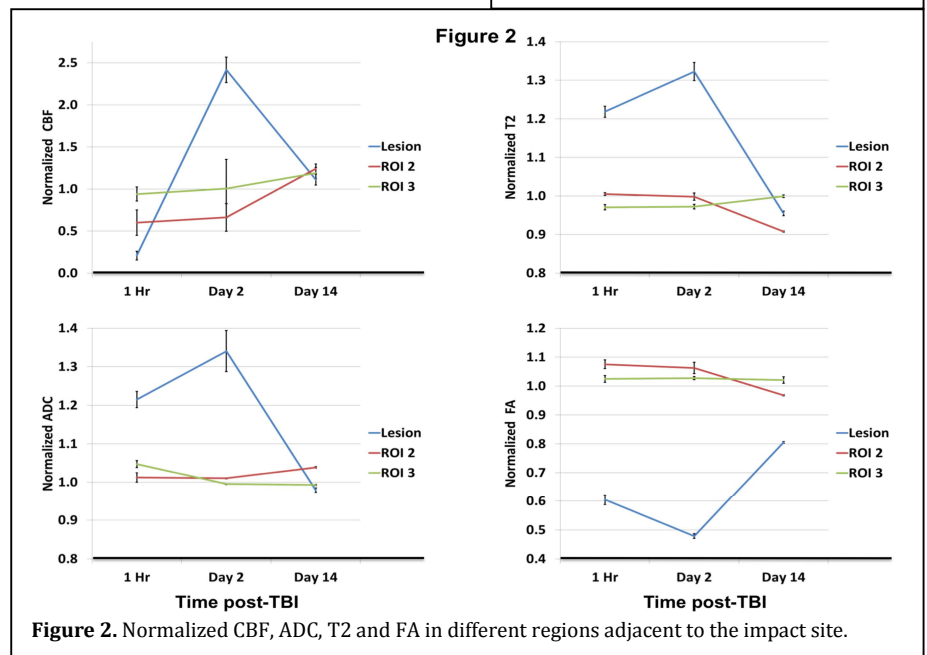


Figure 2. Normalized CBF, ADC, T2 and FA in different regions adjacent to the impact site.