

Longitudinal functional connectivity changes in mild traumatic brain injury: correlation with diffusion, T2 and behavioral outcomes

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Target Audience Researcher in traumatic brain injury using rsfMRI

Purpose Traumatic brain injury (TBI) is a leading cause of death and disability [1]. The goal of this study was to longitudinally examine rsfMRI changes in mild TBI of the (unilateral) primary somatosensory cortex in rats during the hyperacute and chronic phases up to 14 days. Quantitative correlations were made with T2, DTI, fractional anisotropy (FA), and functional outcomes (forelimb placement asymmetry and foot fault scores).

Methods Male SD rats (250-350g, n=5 for controls (no TBI) and 5 for TBI) were studied. A small hole was created over the left forelimb somatosensory cortex (S1), exposing the dura matter. The intact dura matter was impacted with a 3mm tip (5.0m/s, 250µs dwell time, 1mm depth) [2]. Behavioral assessments (foot fault and forepaw asymmetry) were made 1-3 days prior to TBI and again 1, 2, 7, and 14 days post TBI prior to MRI. MRI was performed 1-3hrs, 1, 2, 7 and 14 days after TBI. The 14-day endpoint was chosen based on a subset of studies in which no apparent differences in lesion volumes between 14 and 28 days post TBI were observed. Comparison was made with xx normal, non-TBI animals.

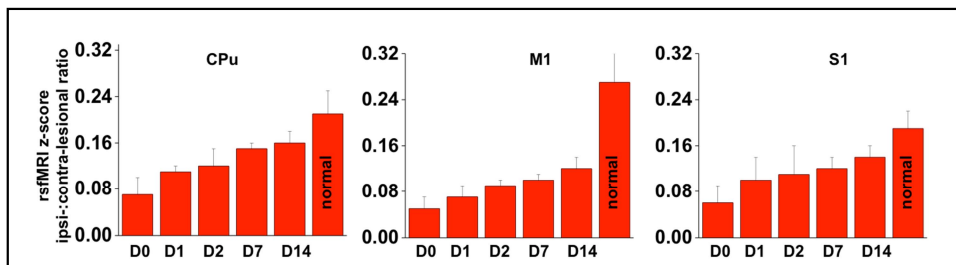


Figure 1. rsfMRI at different time points after TBI. The last bar on each plot was from a separate group of normal animals.

MRI was performed on a 7T under 1.2% isoflurane. Multislice conventional T2 and DTI were obtained for seven 1-mm thick coronal images, FOV=2.56x2.56cm, matrix=96x96 [3]. Images were co-registered. rsfMRI z-scores were obtained using seeds placed in the primary forelimb somatosensory cortex (S1), primary motor cortex (M1), and caudate putamen (CPu) of the ipsi- or contralesional hemisphere. The rsfMRI z score ratios of ipsi:-contra-lesional ROI were determined. Using the same ROIs, T2, ADC and FA differences between ipsi- and contralesional hemispheres were tabulated. rsfMRI z-scores were correlated against T2, ADC, FA, foot fault and forepaw asymmetry scores for days 1 through 14.

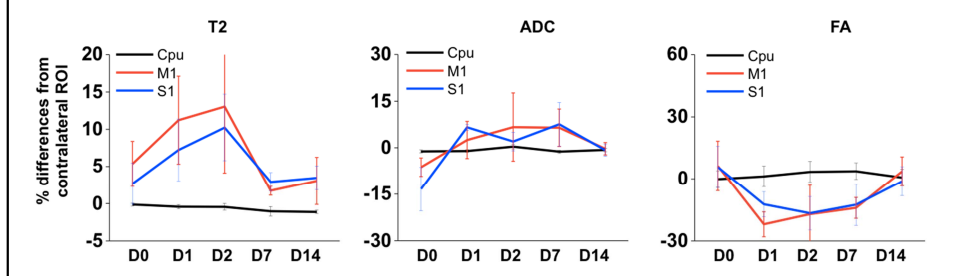


Figure 2. T2, ADC and FA differences from contralesional hemisphere ROI at different time points

Results and Discussion In TBI animals, the z-score ratio of the ipsi- to contra-lesion ROI was markedly smaller compared to non-TBI animals but recovered slowly over time in S1, M1 and CPu but did not reach normal values (Figure 1).

Figure 2 shows the ipsilesional T2, ADC and FA % changes relative to contralesional ROI. T2, ADC and FA showed the biggest difference on day 2 after TBI in S1 and M1, but not in the CPu. The poorest forelimb asymmetry and foot fault scores occurred on day 1 after TBI (Figure 3), indicating sensorimotor deficits following TBI, but recovered substantially by day 7 and 14.

rsfMRI z-scores were correlated with T2, ADC, FA, forepaw asymmetry scores and foot fault scores across all time points (Table 1). Statistically significant correlations were found between rsfMRI and foot fault, and between rsfMRI and forelimb asymmetry in the S1 and M1, but not in the CPu.

Conclusions rsfMRI z-scores reduced after mild TBI but improved with time. The trend of improvement parallels those of behavioral scores. rsfMRI did not significantly correlate with ADC and FA changes, suggesting they provide complementary information. This study demonstrated that rsfMRI offers novel insights into functional connectivity following mild TBI.

References [1] Nortje J, Menon DK, Curr Opin Neurol 2004; [2] Dixon CE, et al., J Neurosci Methods, 1991; 39(3):253-62 [3] Shen Q, et al., J Cereb Blood Flow Metab, 2011; 31, 2076

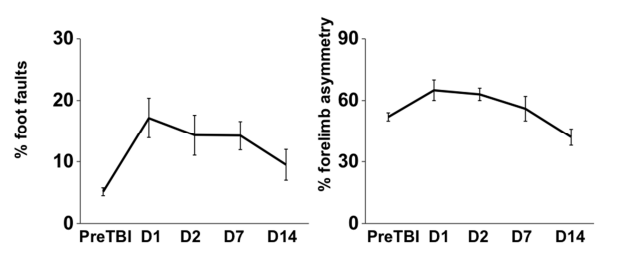


Figure 3. % foot fault and forelimb asymmetry.

		ADC	FA	T2	foot fault	asymmetry
rsfMRI Z-score	CPu	NS	NS	0.01	NS	NS
	M	NS	NS	NS	0.03	0.06
	S1	NS	NS	NS	0.03	0.02

Table 1. P values showing significant correlation rsfMRI z-score with other measures. NS: not significance.