Resting-State Functional Magnetic Resonance Imaging Connectivity and Behavioral Outcomes in Traumatic Brain Injury

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Target Audience: Researcher in traumatic brain injury using resting state functional magnetic resonance imaging

Purpose: Resting state functional MRI (rsfMRI) studies have reported disrupted functional connectivity after traumatic brain injury (TBI) in humans. The types, time after injury, extent and location of TBI in humans are heterogeneous. Animal models of TBI offer a means to study the effects of injury on rsfMRI under controlled conditions. The goal of this study was to use independent component analysis (ICA) method to investigate longitudinal changes in functional connectivity following moderate traumatic brain injury in rats. The impact was targeted to the left primary forelimb somatosensory cortex. Comparisons were made with functional outcomes measured by forelimb placement asymmetry and foot fault behavioral tests.

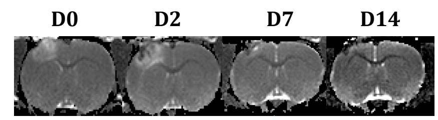

Fig. 1 T2 maps after TBI

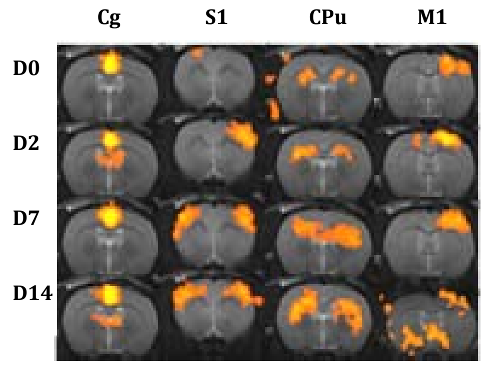

Fig. 2 Group functional connectivity maps.

Methods: An open-skull, controlled cortical impact (CCI) model was used to mimic a moderate TBI in anesthetized rats (250-350g, n=10). 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).[1] Behavioral assessments (foot fault and forepaw asymmetry) were made 1-3 days prior to TBI and again 2, 7, and 14 days post TBI prior to MRI. MRI was performed 0, 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.

MRI was performed on a 7T under 1.5% isoflurane. Multi-slice conventional T_2 images were obtained using fast spin-echo for seven 1-mm thick coronal images, FOV=2.56x2.56cm, matrix=96x96.[2] Resting state images were acquired using gradient-echo EPI with the same geometry and TR/TE=1sec/20ms for 10 mins. Images were co-registered between time points. MELODIC of FSL was used for group ICA analysis.[3] From 20 components generated, only the components corresponding to the cingulate (Cg), primary motor cortex (M1), primary forelimb sensory cortex (S1) and caudate putamen (CPu) regions were analyzed. The normalized number of activated pixels (the number of activated pixels divided by the value of day 0) was calculated. Correlations between rsfMRI results and foot fault or forepaw asymmetry scores were made for days 1 through 14.

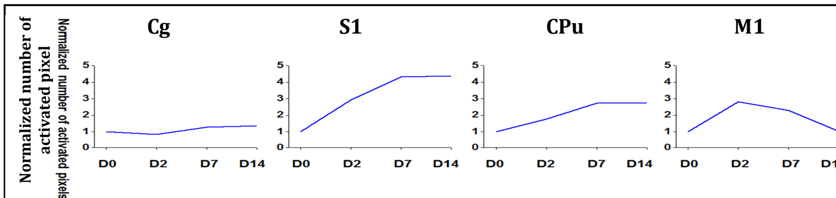

Fig. 3 rsfMRI connectivity at different time points after TBI.

Results: Figure 1 shows representative T_2 maps 0, 2, 7 and 14 days following TBI**.** We identified four reproducible rsfMRI patterns (Cg, S1, M1 and CPu) selected due to their relevance for the injury sites and behavioral tasks implemented (**Figure 2**).

For comparison and quantification, the numbers of activated pixels in the rsfMRI (normalized to day 0) are plotted across time (**Figure 3**). Cg cluster size did not change with time. S1 and CPu cluster sizes grew with time. A transient increase in M1 cluster size was observed on day 2 only. The forelimb asymmetry and foot fault scores peaked on day 2 following TBI (Figure 4).

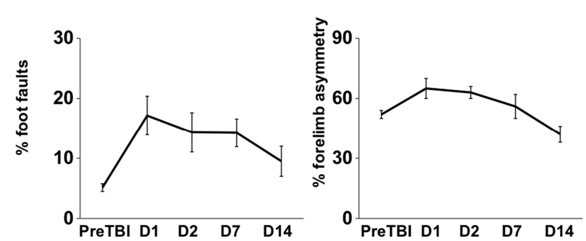

Fig. 4 % foot fault and forelimb asymmetry.

Discussion and conclusions: The Cg is located away from the primary injury site and thus its rsfMRI pattern was not affected significantly. S1 rsfMRI pattern was markedly attenuated on day 0, as expected. The S1 rsfMRI recovered substantially on day 7 and 14, consistent with behavioral scores. The CPu rsfMRI pattern was also affected. This is likely due to the fact that the CPu is functionally connected to the S1. Interestingly M1 rsfMRI patterns did not recover following TBI even though behavioral improved. This is likely due to functional compensation or the utilization of peripheral connectivity networks.

In conclusion, rsfMRI patterns in S1 and CPu were clearly reduced after moderate TBI but recovered with time. The trend of improvement parallels those of behavioral scores. This study demonstrated that rsfMRI offers novel insights into functional connectivity following mild TBI.

References 1. Long JA, et al., J. Neurotrauma. doi:10.1089/neu.2014. 2. Shen Q, et al., J Cereb Blood Flow Metab, 2011; 31, 2076. 3. Beckmann CF, et al., IEEE Trans. Med. Imaging, 2004; 23, 137-152.