

Longitudinal functional connectivity changes in Middle Cerebral Artery Occlusion: correlation with diffusion, T2 and behavioral outcomes

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Audience: Researchers interested in stroke imaging, resting state MRI

Purpose: Following middle cerebral artery occlusion (MCAO) disruption and subsequent reorganization of functional connections occurs within and surrounding an infarct, however the extent of recovery and its correlation with functional outcomes is not fully understood. The goal of this study was to longitudinally investigate functional connectivity with respect to functional recovery following transient (45-minute) MCAO.

Methods: Male Sprague-Dawley rats (250-300g, N=4) underwent 45-min middle cerebral artery occlusion (MCAO) under 1.2% isoflurane. rsfMRI was acquired at 3 hrs and 2, 7, and 28 days post MCAO using a Bruker 7-T/40-cm scanner.¹ Behavioral assessments (foot fault and forepaw asymmetry) were made 1 day prior to MCAO and again 2, 7, and 28 days post TBI. Multislice conventional T2 and DTI were obtained for seven 1.5-mm thick coronal images, FOV=2.56x2.56cm, matrix=96x96, and reconstructed to 128x128.² Resting state images were acquired using gradient-echo EPI with the geometry and TR=1sec, TE=26ms. 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 hemispheres. The rsfMRI z score ratios of ipsi-:contra-lesional ROI were determined. rsfMRI z scores were correlated against apparent diffusion co-efficient (ADC), T2, fraction anisotropy (FA) and behavioral assessments for D0 through D28. For comparison, four normal rats were used to determine normal resting state responses.

Results & Discussion: The z-score ratio of the ipsi- to contra-lesion ROI was markedly smaller compared to normal animals but recovered slowly over time in S1 and M1, but did not reach normal values (Figure 1). The z-score ratio of the ipsi- to contra-lesion in the CPu remained markedly smaller at all time points examined but was accentuated on day 2.

The percent difference of ADC, T2, and FA from the contralesional ROI is shown in Figure 2. ADC of the CPu decreased initially, pseudo-normalized on day 2 and fluctuated on day 7 and 28, which was consistent with the ADC change pattern of an ischemic lesion. S1 and CPu showed elevated T2 on day 2, with the S1 area of some animals being inside the lesion. FA of the CPu was significantly lower than M1 and S1 on days 0 and 2.

Figure 3 demonstrates the functional outcome measures using the asymmetry and foot fault tests. MCAO caused significantly increased utilization of the non-affected limb on Days 2 and 7, and returned to Pre-MCAO values by day 28. In addition, foot faults scores were significantly higher on days 2, 7 and 28 post-MCAO indicating impairment in motor function of the left forepaw. The insets show that the activity level was significantly impaired following MCAO.

The correlation between rsfMRI z-scores and structural data (T2, ADC, FA), or functional outcomes (forelimb asymmetry or foot fault scores) were calculated across all time points (Table 1). Significant correlations were only found between rsfMRI and asymmetry outcome measures in the S1 and CPu, but not in M1. There were no statistical correlations between rsfMRI and foot fault scores likely due to the inactivity of the animal during the tests in the first 48 hours. No statistical correlations were found between rsfMRI and ADC, T2 or FA.

Conclusion: rsfMRI z-scores decreased following MCAO but improved with time. The trend of improvement correlated with asymmetry behavioral scores. rsfMRI did not significantly correlate with ADC, FA and T2 changes, suggesting they provide complementary information. These findings will help to provide insight into functional connectivity and reorganization following MCAO based on MRI data.

References: 1) Shen et al., 2003 JCBFM 23:1479-1488; 2) Shen Q, et al., JCBFM, 2011; 31, 2076

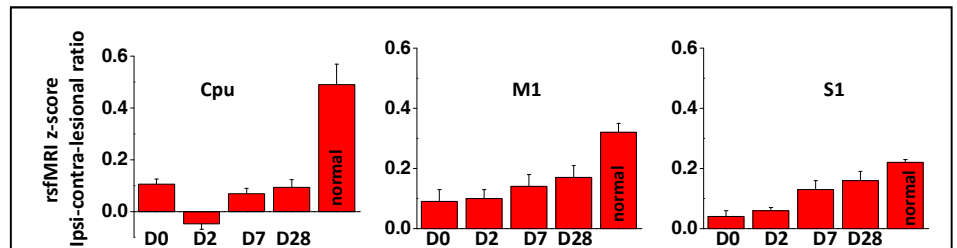


Figure 1. rsfMRI z-score ipsi-:contra-lesional ratio on day 0, 2, 7 and 28 post-occlusion in different regions. For comparison, results of a group of normal animals (N=4) are also shown.

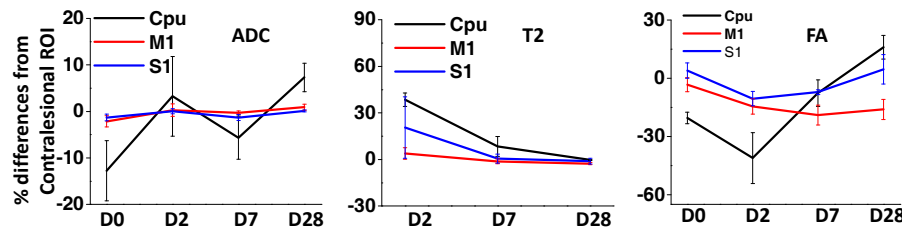


Figure 2. ADC, T2 and FA changes over time in ipsi-lesional CPu, M1 and S1 regions. The values were expressed using percent differences from contra-lesional ROIs.

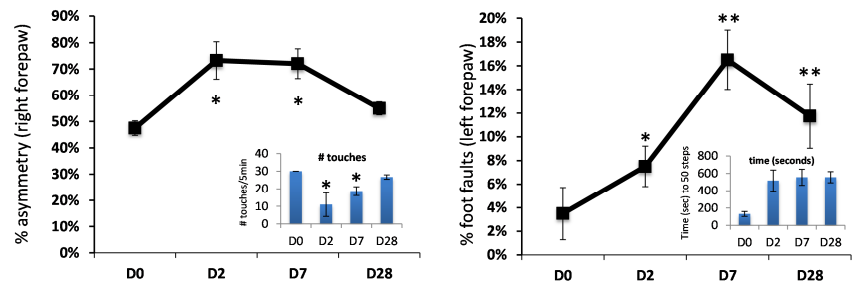


Figure 3. Asymmetry and foot fault behavioral outcomes following MCAO. Insets show the activity of the animals in each test demonstrating decreased motor and exploratory behaviors.

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

	ROI	ADC	FA	T2	foot fault	asymmetry
rsfMRI z score	S1	NS	NS	NS	NS	0.008
	M1	NS	NS	NS	NS	0.1
	CPu	NS	NS	NS	NS	0.08