Temporal and Spatial Evolution of MR derived cerebral metabolic rate of oxygen utilization index in acute Middle Cerebral Artery Occlusion Stroke rats

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Introduction

It has been suggested that cerebral metabolic rate of oxygen utilization (CMRO2) is a critical physiological parameter for insights into tissue viability[1] during acute cerebral ischemia. The main purpose of this paper is to study the temporal and spatial evolution of MR measured cerebral metabolic rate of oxygen utilization index (MR_COMI), a parameter that provide similar information as the CMRO2 defined in PET literature, and its correlation with the final tissue outcome defined by T2 images acquired at 24 hours after MCAO in an middle cerebral artery occlusion (MCAO) rat model.

Method

Cerebral ischemia was induced in-bore using an intraluminal suture MCAO model in thirty-two rats with approved protocols. MR images were acquired on a Siemens 3T Allegra scanner with a small animal coil. A two-dimensional multi-echo gradient echo/spin echo sequence was utilized to estimate oxygen extraction fraction (MR-OEF)[2] prior to and continued up to 90 minutes post MCAO with an interval of 15 minutes. A segmented EPI DSC perfusion weighted imaging (PWI) was utilized to estimate cerebral blood flow (CBF) 90 minutes after MCAO so as to avoid the contamination of the susceptibility induced by the contrast agent upon MR-OEF measurements. Since an intraluminal suture MCAO was used in this study, CBF was assumed to remain constant for the entire 90 minute imaging session. Immediately after the imaging session, the suture was withdrawn from MCA to restore CBF for reperfusion. T2-weighted images acquired at 24 hours after MCAO were rigidly co-registered onto the images obtained at the acute stage with FSL 3.2 (FMRIB, Oxford, UK). Final T2 lesion was defined as the hyper-intensity regions (greater than mean + 2 * SD of the signal intensity in the contralateral hemisphere). CBF lesion is defined as the region in the ipsilateral hemisphere with CBF values less than the mean minus 1SD of the CBF in the ROI in the contralateral hemisphere. MR-CMRO2 ratios from three different ipsilateral ROIs (matched CBF/T2 lesion, mismatched CBF/T2 lesion and without CBF/T2 lesion) over their counterparts in the contralateral hemisphere were obtained every 15 minutes. In addition, a histogram analysis was employed in the matched CBF/T2 lesion and its peri region (n=22) every 15 minutes.

Results

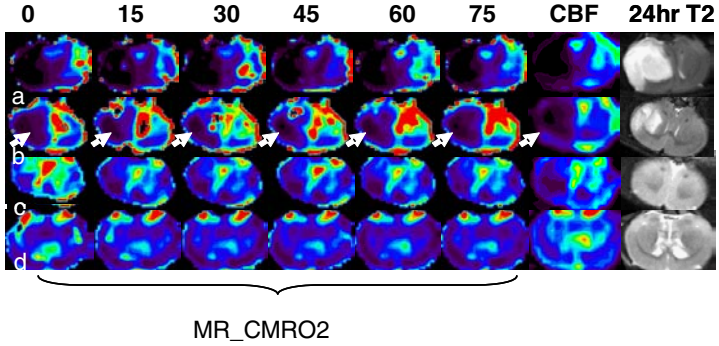

Figure 1. Representative temporal evolution of CMRO2 (first 6 columns), CBF (7th column) and final T2 maps (the last column) for four rats.

Among all rats, 22 rats developed both CBF and T2 lesion (matched CBF/T2 lesion), rats only showed CBF lesion without final T2 lesion (mismatched CBF/T2 lesion) and 6 rats had neither CBF nor T2 lesion (without CBF/T2 lesion). Figure 1 showed results obtained from four representative rats that exhibit various degree of ischemic injuries. The severity was progressively decreased from rows **a** to **b** and rows **c**-**d** had no visible T2 lesions. In row **a**, MR_CMRO2 was markedly reduced immediately after MCAO and throughout the entire ischemic duration. In contrast, a spatially progressed lesion (arrow) was observed in row b. Row **c** showed a rat with an acute CBF lesion but without the final T2 lesion. The mild reduction of MR_COMI suggested a reversible lesion, which was confirmed by the 24 hour T2. Row **d** had no lesion in both CBF and T2 maps, and a comparable MR_COMI was obtained in both hemispheres.

These results demonstrated that the proposed approach for obtaining MR_COMI was highly effective in delineating a different degree of ischemic injuries. The means and standard deviations of the temporal evolution of MR_COMI from the previously defined three types of ROIS were given in Figure 2. During the entire 90 minutes, statistically significant differences were observed between the MR_COMI from matched and mismatched CBF/T2 lesion and its counterpart from the without CBF/T2 lesion (**p<0.001). Figure 3 showed the histogram analysis of the T2/CBF matched regions at three different times during MCAO and that in the peri-lesion region. The peaks of the three histograms obtained from the matched T2/CBF ROI appear to be independent of the ischemic duration, suggesting that the mean MR_COMI is stable throughout the entire MCAO duration. The shoulder (solid arrow) for the 0-15 min histogram becomes less apparent and appears to be left shifted in the 30-45min histogram, suggesting that more pixels evolve from a higher to lower MR_COMI. This behavior is even more apparent for the 75-90min histogram (dashed arrow). Finally, the histograms between the T2/CBF matched and peri-lesion regions are well separated.

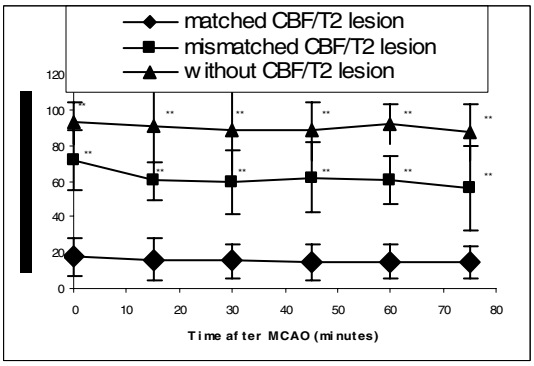

Figure 2. Temporal evolution of MR-CMRO2. The error bars represent the inter-subject variation. Significant differences were observed between the matched CBF/T2 lesion and the mismatched and without CBF/T2 lesions (** stands for p<0.001)

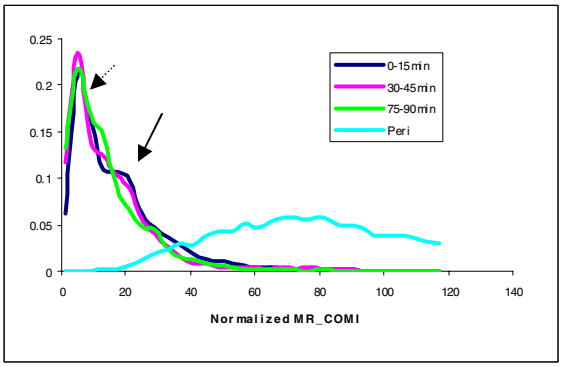

Figure 3. Histogram analysis of the T2/CBF matched regions at three different times during MCAO along with the histogram in the peri-lesion (Peri) region.

Discussion and Conclusions

The capability of identifying salvageable tissue is critically essential. CMRO2 is important in providing vital information for tissue viability during acute cerebral ischemia. With the MCAO rat model, we have demonstrated the MR_COMI capable of revealing the temporal and spatial evolutions of ischemic lesions. Lesions recruited to final infarction usually have a substantial reduction in MR_COMI, while the reversible lesions only show modest reduction in MR_COMI. In addition, cerebral tissue without CBF/T2 lesion demonstrates a similar MR_COMI between the ipsi- and contra-lateral hemispheres. In summary, MR_COMI exhibits a similar evolution as those reported using PET[3] and the consistency between MR_COMI and final T2 delineated lesion suggests the potential clinical utility of MR_COMI.

Reference

1. Powers et al. *JCBFM*. 1985;5:600, 2. An and Lin, JCBFM, 2000, 20:1225. 3. Young et al, JCBFM, 1996, 16,1176.