fMRI of Focal Ischemia model of Stroke in the Rat Whisker Barrel Cortex

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INTRODUCTION Stroke results in interrupted microcirculation in the infarct area and reduced perfusion in the surrounding areas. These changes can be expected to lead to reduced hemodynamic response to stimulation. We hypothesize that fMRI signal magnitude and activation area will be modulated by the reduced hemodynamic response. We use fMRI to test this hypothesis in a rat stroke model.

An occlusive stroke model in rat barrel cortex has been reported elsewhere (1). This model induces stroke by cauterizing the specific branches of the middle cerebral artery that feed the whisker barrel cortex. A challenge in functional imaging of this animal model is that severe susceptibility artifacts from surgery essentially preclude the use of regular gradient-recalled EPI (GR-EPI) sequences. We report here the strategies that have been employed to deal with this problem. Results suggest that interleaved asymmetric spin echo (SE) EPI is a practical way to minimize susceptibility-induced signal dropout, and that CBV-weighted fMRI employing exogenous iron oxide contrast agent is an effective way to improve functional sensitivity.

METHODS **1. Animal Preparations**. Permanent focal ischemia was induced by electrically cauterizing critical arteriolar branches of the middle cerebral artery around the barrel cortex through a cranial window. After 72 hrs, rats were artificially ventilated and scanned at a 3T scanner under α-chloralose anesthesia. A water-heating pad was used to keep body temperature within normal ranges. **2. Imaging Methods**: (i) Interleaved GR/SE and asymmetric SE-EPI sequences employing phase-encoded reference scans for phase corrections (2); (ii) High efficiency local gradient coil (20 G/cm/100A along X and Y, 40 G/cm/100A along Z) and RF coils (3); (iii) in-house-made whisker stimulator for *bilateral* whisker stimulations. Stimulus paradigm was a block design consisting of 4 cycles of 80 s off and 64 s on, and a frequency of 12 Hz; (iv) Low resolution BOLD and CBV-fMRI (TR = 1~4 sec, TE = 18~27 ms, FOV = 3.5 cm, slice thickness = 2 mm). High resolution CBV-fMRI (asymmetric SE-EPI, TR = 4 s, TE = 40 ms, FOV = 2 cm, matrix = 96 × 96, slice thickness = 2 mm); (v) Data were analyzed using AFNI (4).

RESULTS

1. The arrow in Fig. 1a indicates signal dropout. This image was acquired using 4-shot GR-EPI with a TE of 15 ms. Susceptibility-induced signal dropout can be clearly visualized. However, as expected, the signal was substantially recovered with 4-shot SE-EPI (Fig. 1b). There were two regions of low signal intensities in Fig. 1b. These regions were believed to be infarct tissue.

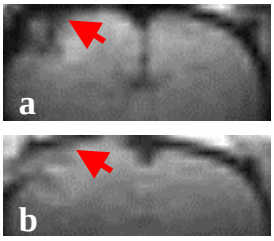

Fig 1. Comparison of susceptibility effect using 4-shot GR-EPI and SE-EPI.

2. BOLD fMRI with *bilateral* whisker stimulation. The left barrel cortex was infarcted while the right barrel cortex was intact, as shown in the anatomical images (Figs 2a-b). Figures 2c-d show BOLD activation maps ($p<0.05$) using asymmetric SE-EPI (Δ_{TE} = 5ms). Both the magnitude and area of BOLD response in the infarct side were significantly reduced.

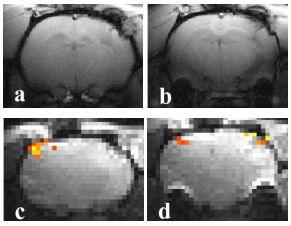

Fig 2. BOLD cross-correlation activation maps in the infarct and normal sides.

3. CBV-fMRI. MION was injected (12mg/kg) to enhance functional sensitivity. Figure 3a shows an activation map ($p<0.01$). The barrel cortex in the normal hemisphere exhibits greater response. More importantly, the infarct side also shows functional signal in response to whisker stimulation. The arrow in Fig. 3b indicates infarct area.

4. Fig.3c shows a triphenyltetrazolium choloride (TTC) staining in the barrel cortex. Comparable section of the brain was incubated in 2% TTC for 15 minutes. Arrow indicates infarct regions.

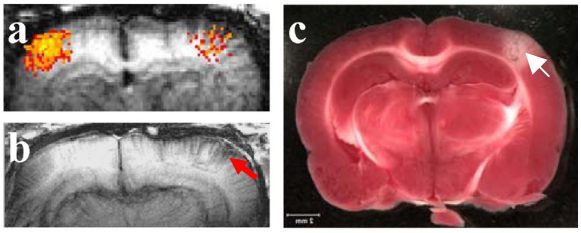

Fig 3. a: CBV-fMRI activation maps. Matrix 96 × 96, FOV 2 cm, 2 mm slice thickness. b: EPI anatomical image of a. arrow indicates infarct area. c: TTC staining of the comparable section.

DISCUSSION BOLD and CBV-weighted fMRI can be used to investigate stroke-related functional activity. High resolution has been demonstrated using CBV-fMRI in this animal model. Interleaved asymmetric SE-EPI is a practical way to deal with susceptibility due to surgery in this animal model.

REFERENCES 1. Forder JP *et al*. Focal ischemia model of stroke in the rat. FASEB 2003;Poster#4146. 2.&3. Lu H *et al*. Magn Reson Med (in press). 4. Cox RW *et al*. NMR Biomed 1997;10:171-178.