Interhemispheric Connectivity in MEMRI Correlates with Interhemispheric in Resting-state fMRI

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INTRODUCTION: Resting-state functional connectivity MRI (RSfcMRI) is the measure of spontaneous fluctuations in BOLD signal. It has been previously suggested that RSfcMRI reflects neural networks [1]. Manganese ion can enter excitable cells via voltage-gated calcium channels, hence manganese-enhanced MRI (MEMRI) has been widely used for measuring the neuronal activity and for tracing neuronal pathways [2, 3]. In this study, both MEMRI and RSfcMRI were employed to investigate functional and structural interhemispheric connections in the visual cortex of rodent model.

MATERIALS AND METHODS: Animal Preparation: Male adult Sprague-Dawley rats (320 – 350g, 3 months, N=3) were examined using RSfcMRI. 3 days later, 108nl Mn^{2+} (100mM, pH=7.4) was injected into the visual cortex (6.5mm posterior to bregma, 4mm from the brain midline and 1.8mm from the cortical surface). MEMRI data was acquired 24 hours after the injection. All animals were under mechanical ventilation during MRI experiments with 1.5% (RSfcMRI) and 2.0% (MEMRI) isoflurane anesthesia. **MRI Protocol:** All MRI data was acquired with the 7 T Bruker scanner using a surface coil. RSfcMRI data was acquired using a single-shot GE-EPI sequence with TR/TE=1000/20ms, flip angle=56° , FOV=32×32mm^2, MTX=64×64, 10 1mm slices and a total of 400 data points. MEMRI data was acquired using T1-weighted MDEFT sequence with RI/TR/TE=1100/12/4ms, FOV=32×32mm^2, MTX=64×64, 16 1mm slices, 4 segments and 8 averages. RARE T2W images were acquired with TR/TE=4200/36ms as anatomical reference for MDEFT and EPI images. **Data Analysis:** All MEMRI images were co-registered using T2-weighted images as a reference. A 4×4 seed voxels was placed near the injection site and its signal intensity was used to normalize the T1-weighted MDEFT images. A region of interest (ROI) was defined in the visual cortex. Signal intensities of the voxels within the ROI were extracted for quantitation in the visual cortex. All RSfcMRI data were compensated for slice timing, detrended, realigned as well as temporally low-pass filtered to obtain low frequency fluctuations. Subsequently, inter-animal co-registration was performed using their respective T2-weighted image as a reference. Correlation coefficient maps were obtained using seed based analysis (SBA) with a 4×4 seed voxel on the injection site. The correlation coefficients in the ROI were extracted for quantitation in the visual cortex.

RESULTS: Fig.1 shows the typical T2-weighted image overlaid by the rat brain atlas showing the location of seed voxel in Mn injection site V1 and the contralateral ROI. Fig.2 shows the typical manganese-enhanced T1-weighted image with the Mn injection site, seed voxel and ROI depicted. Fig.3 shows the contralateral side of the normalized manganese-enhanced image (left) and the correlation coefficient maps overlaid on T2-weighted image (right). Fig.4 shows the scatter plots of each individual animal and the average of all animals. The results clearly indicated the correlation between the normalized signal intensities in MEMRI and functional connectivity in RSfcMRI.

DISCUSSION AND CONCLUSION: Mn transport is activity-driven and occurs via both axonal connections and neuron synapse terminals [4]. MEMRI has been used to visualize the interhemispheric connectivity between cortices [3]. The results in Fig. 4 showed strong correlation between normalized signal intensities in MEMRI and correlation coefficients in RSfcMRI. The results suggested that a tight coupling exist between structural and functional connections in the bilateral visual cortex. Hence, MEMRI in conjunction with RSfcMRIcan be used for investigating different biomedical studies.

REFERENCES: 1. Fox MD, Nat Rev Neurosci. 2007. **2.** Canals S, Neuroimage 2008 **3.** Inoue T, J Neurosci. Rev Neurosci 2011 **4.** Silva AC, Neuroimage. 2012

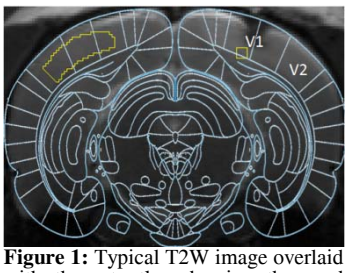

Figure 1: Typical T2W image overlaid with the rat atlas showing the seed voxels and region of interest.

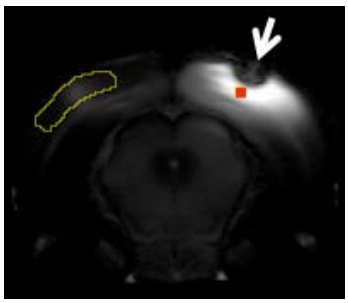

Figure 2: Typical manganese enhanced T1W image with the manganese injection site (arrow), seed voxels (red) and region of interest.

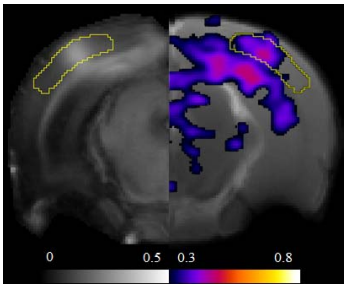

Figure 3: Mean manganese-enhanced T1-weighted image and mean correlation coefficient map overlaid on the T2-weighted image of the contralateral side of the injection site (V1).

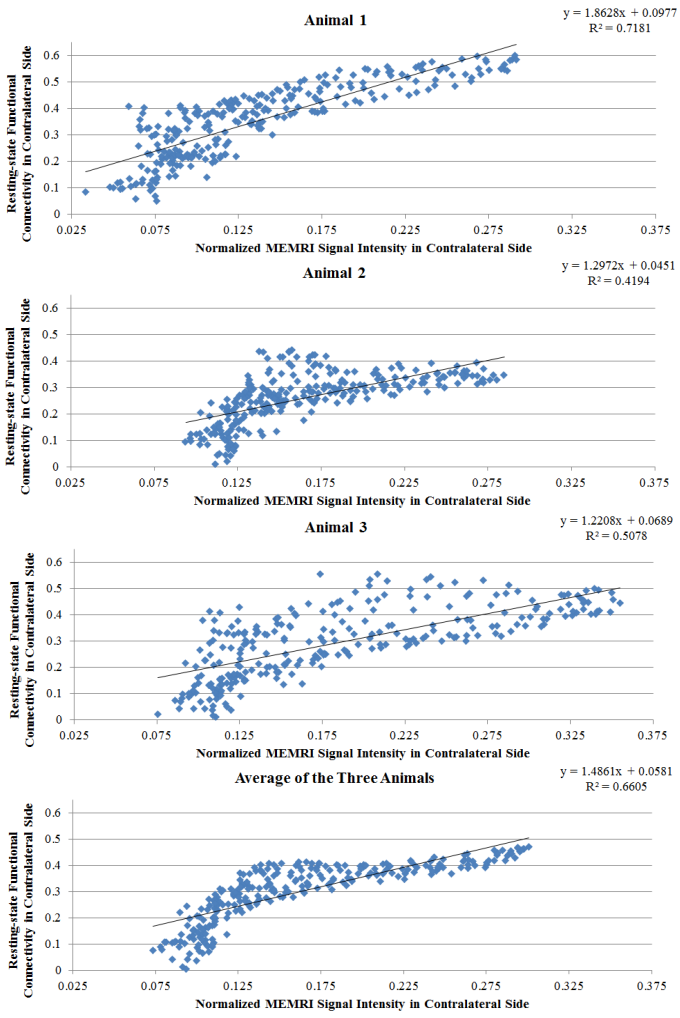

Figure 4: Scatter plots of resting-state functional connectivity against manganese-enhanced T1-weighted signal intensities of the contralateral visual cortex in each individual. The scatter plot of the average is also shown.