MRI evidence of resting state connectivity in rodent brain

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Introduction

Correlations have been observed in fMRI time courses from functionally related regions of the human brain while at rest, but the implications of these correlations for brain function are unclear [1,2]. Extension of functional connectivity studies to the rodent would enable a more thorough investigation into this phenomenon. This work looks for evidence of resting state connectivity in the rat brain with the ultimate goal of using behavioral and biochemical techniques to probe the origins of these correlations.

Method and Materials

Six rats were intubated, mechanically ventilated, and anesthetized with α-chloralose. Each rat was imaged on a Bruker 11.7 T scanner using a single-shot gradient-echo EPI sequence to acquire T_2*-weighted MR images with the following parameters: 64 x 64 matrix, effective echo times 13, 17, 20, 25, 30, and 35 ms, repetition time 100 ms, bandwidth 200 kHz, field of view 1.92 x 1.92 cm, with one 2 mm coronal slice covering the bilateral primary somatosensory cortex. Each series consisted of 1200-3600 images. Images were acquired with different echo times to determine optimal sensitivity to the low frequency resting state fluctuations previously seen in human studies. Activation maps were also acquired during electrical stimulation of the forepaw in order to identify the primary somatosensory cortex (SI). Power spectra were obtained from SI, the sagittal sinus, and a region outside the brain. In the resting state data, a region of interest (ROI = 2 x 2 pixels) was chosen in SI and the time course from the ROI was low-pass filtered and correlated with the time courses from all other pixels in the brain to make a resting-state correlation map.

Results

The power spectra from SI show structure in the low frequencies (<0.2 Hz) that is not present in the spectra from the sagittal sinus or outside the brain. Peaks corresponding to respiration (~1 Hz) and cardiac pulsation (~4-5 Hz) can be seen in some spectra, particularly from the sinus (Fig. 1). The presence of the low frequency peaks suggests that resting state fluctuations similar to those observed in humans are also present in rats. Correlation maps created after low-pass filtering using a seed in SI demonstrate increased correlation in the cortex, especially in the primary and secondary somatosensory regions and motor region (average correlation coefficient = 0.60 +/- 0.12), compared to subcortical structures (average correlation coefficient = 0.09 +/- 0.06) (Fig. 2). Previous studies have demonstrated the echo time dependency of the human resting state signal [2, 3]. This TE dependency was similarly observed in the present animal data, in which a shorter echo time (TE=15 ms) improves the global signal-to-noise ratio and decreases the distortion seen in the image, but a longer TE (TE = 35 ms) provides more sensitivity to tissue specific T_2* effects (Fig. 3). T_2* of the rat cortex at 11.7 T is about 25 ms, and typical BOLD-weighted studies use TEs in the range of 15-25 ms, depending on distortion and signal loss. To optimize visualization of activation in the cortex, several frequency cutoff values were used for the low-pass filter frequency (0.01-0.20 Hz). A frequency cutoff of 0.14 Hz was chosen to process images. Average correlation values were based upon a user-chosen ROI (3 x 3 pixels) in the generated correlation map.

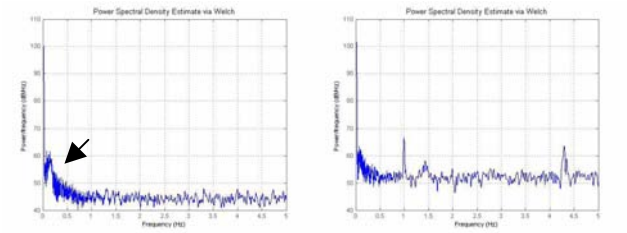

Figure 1. Power spectral density estimate from pixel in SI, arrow indicates the low frequency peak discussed in text (A); data from the base of the brain shows low frequency peak as well as cardiac (4.3 Hz) and respiratory peaks (B).

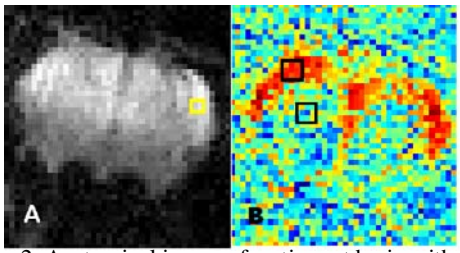

Figure 2. Anatomical image of resting rat brain with selected ROI for correlation indicated in yellow (A) next to correlation map generated (B). The black squares indicate example ROIs selected to generate correlation averages in comparing cortical vs. subcortical regions.

Discussion

This study demonstrates evidence of resting state connectivity in the rodent brain. In the coronal slice used for this study, the resting state connectivity was highest between the ROI in SI, contralateral SI, and the motor cortex. In some rats, strong connectivity was also seen with bilateral SII (not shown). In contrast, the connectivity was lower in subcortical structures such as the thalamus. Future studies will include the acquisition of transverse images of the brain to determine cortical localization of the low-frequency functional connectivity over larger anatomical distances. The connectivity observed in this study paves the way for future experiments that may elucidate the connection between functional connectivity and brain function.

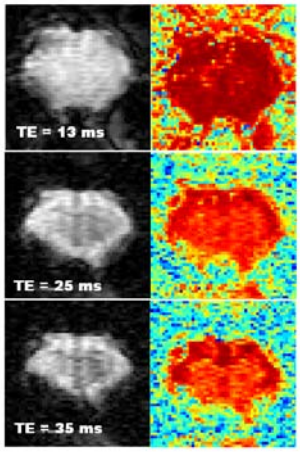

Figure 3. Although SNR is reduced, correlation differences between the cortex and subcortical structures are better visualized at long TE.

References: 1. Biswal B, Yetkin FZ, Haughton VM, Hyde JS. *MRM* 1995;34:537-541. 2. Peltier SJ, Noll DC. *NeuroImage* 2002;16:985-992. 3. Hyde J, Biswal B. Functionally related correlation in the noise, In *Functional MRI*, pp 263-275. Springer-Verlag, Berlin, 2000.