Functional Connectivity Mapping in the Rat Brain using Spin-echo EPI

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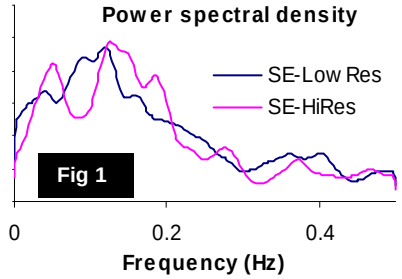
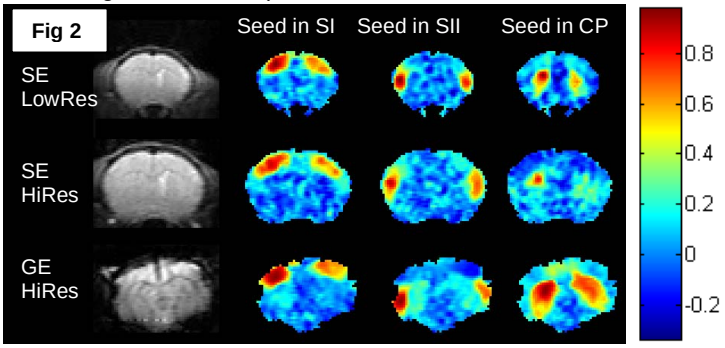
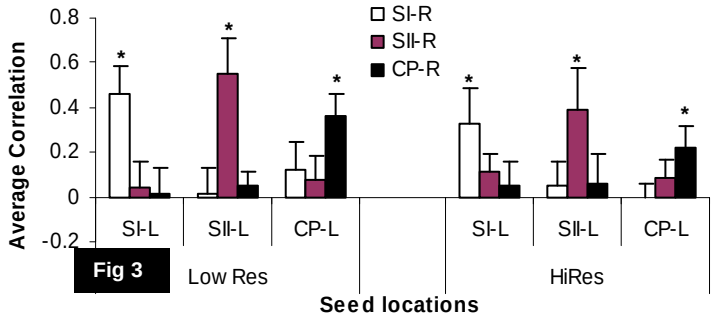
Introduction: Low frequency fluctuations (LFFs) in T2*-weighted MR images have been used to map functional connectivity in both humans and rats [1, 2, 3]. Most FC studies utilize gradient echo EPI (GE-EPI) because of its high sensitivity to BOLD signal fluctuations. However, fMRI studies have shown that the BOLD signal in GE-EPI images contains a strong contribution from large veins. At high fields, spin echo EPI (SE-EPI) provides functional contrast which is predominantly caused by microvasculature, and gives better functional specificity [4]. Also, SE-EPI images are less susceptible to geometric distortion and signal loss due to magnetic field inhomogeneities [5]. This study uses a rat model to demonstrate that FC maps comparable to those obtained using GE-EPI can be obtained using SE-EPI.

Methods: Imaging was performed on 9.4T Bruker scanner. The rats (n = 6) were sedated using medetomidine as described in [3]. For each rat, a series of SE-EPI images was acquired of a single coronal slice covering somatosensory cortex with following parameters: TR = 1000 ms, TE = 30-40 ms, 64x64 matrix, in-plane resolution = 400 microns, 1mm slice thickness, 250 repetitions. For 4 of the rats, SE-EPI image-series with in-plane resolution of 300 microns were also acquired. For convenience, scans with in-plane resolution of 300 microns and 400 microns are referred to as LowRes and HiRes scans respectively. All the images in the series were blurred using a 3x3 Gaussian kernel with $\sigma = 2$ pixels. Power spectral density estimates for time-series corresponding to primary somatosensory cortex (SI) were obtained using Welch method after discarding transient time-points, detrending and de-meaning. Individual time-courses were filtered using a low-pass filter ($f < 0.2$ Hz), followed by quadratic de-trending. Seeds (5x5 for HiRes, 3x3 for LowRes) were placed in left SI, secondary somatosensory cortex (SII) and caudate-putamen (CP) and cross correlation maps were obtained. ROIs were manually drawn in right SI, SII and CP to compute average cross correlation values of all the seeds with these regions. T-test was performed on the average values obtained from different rats to detect the correlation values significantly different from zero. We also made qualitative comparison between these FC maps with those obtained with using GE-EPI data (n = 6, TR = 100 ms, 1 mm slice thickness, in-plane resolution = 300 microns, 3600 repetitions).

Results: Fig 1 shows power spectra (averaged over the datasets) of signal obtained from SI. High power in low frequency region can be observed. Fig 2 shows cross-correlation maps obtained from a LowRes SE-EPI dataset, a HiRes SE dataset and a HiRes GE dataset. SE-EPI FC maps show connectivity patterns similar to those observed for GE-EPI. Three networks (consisting of bilateral SI, SII and CP respectively) are seen. Fig 3 shows average correlation values in selected ROIs for seeds placed in different locations (shown for SE datasets. SI-L and SI-R mean left and right SI respectively, and so forth). Asterisk ('*') means that the corresponding correlation coefficient is significantly different from zero ($p < 0.05$). Clearly, SI, SII and CP show significant correlation with bilaterally symmetric regions only, suggesting the presence of three distinct networks. Reduced correlation is observed for HiRes SE-EPI datasets due to lower SNR.







Our results demonstrate that SE-EPI is sensitive to BOLD fluctuations in rat brain with TE as short as 30 ms and an in-plane resolution of 300 microns. Although SE-EPI does not allow TR short enough to avoid aliasing of physiological noise, the patterns we observed are identical to those obtained for GE-EPI data with TR short enough to avoid aliasing of primary components of physiological contributions. SE-EPI is expected to provide functional contrast that originates almost exclusively from microvasculature [4]. Therefore, our results imply that the microvasculature has a significant contribution towards coherent LFFs in BOLD. The spatial extents of seed-based correlation maps were similar for both GE-EPI and SE-EPI. A major advantage of using SE-EPI for FC studies is that SE-EPI images suffer from less geometric distortion (fig 2) and are relatively less sensitive to magnetic field inhomogeneities. It is difficult to acquire GE-EPI images from the entire brain without observing significant signal dropout and image distortion in some slices, but whole-brain imaging is readily feasible with SE-EPI. SE-EPI's reduced sensitivity to magnetic field inhomogeneities is also critical for future work combining electrophysiology and fMRI, as electrodes placed in or near the cortex create severe signal dropout..

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