DIFFERENTIATING NEURONAL AND NON-NEURONAL CONTRIBUTIONS IN BOLD SIGNAL USING MULTIMODAL RECORDINGS AND MULTI-ECHO EPI

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Target audience: Researchers and clinicians utilizing fMRI and/or EEG to study spatiotemporal dynamics of the resting human brain in healthy and diseased states.

Introduction: A critical challenge in the BOLD fMRI based study of functional connectivity is distinguishing neuronally originated signal from the effects of motion, physiology, and other nuisance sources. Recent studies have suggested that the differentiated tissue-dependent signal decay as measured by multi-echo (ME) echo-planer imaging (EPI) may reveal BOLD signal of neuronal or non-neuronal/physiological origin [1-3]. Here we have acquired single shot ME gradient echo EPI (geEPI) with Sensitivity Encoding (SENSE) [4] simultaneously acquired with EEG, and physiological data (respiration). We decompose the multi-echo EPI data into independent components using the spatial independent component analysis (ICA) and components of neuronal or non-neuronal origin were identified by comparing with temporal dynamics of the multimodal data (i.e. EEG, and respiration), based on which BOLD physiological noise contribution can be identified and be removed.

Methods: Four healthy human subjects (age 43 ± 6 years; one female) participated in the study. The experiments were performed on a General Electric Discovery MR750 3T MRI scanner with an 8-channel receive-only head array coil. For the whole brain fMRI, a single shot multi-echo EPI sequence with Sensitivity Encoding (SENSE) was used (image matrix=64×64, acceleration=2, FOV/slice thickness/gap=240/3.7/0.3mm, *TR/TE1/TE2/TE3*=2500/14.1/36.6/59.1ms, flip=30°, 31 axial slices, and 150 volumes). High-density EEG signals from 32 channels were simultaneously recorded with BOLD fMRI scans using MRI-compatible BrainAmp MR Plus amplifiers (in 0.016–250 Hz band with 0.1 μV resolution and 5000 Hz sampling rate). Subjects were asked to rest with their eyes closed or open (looking at a fixation cross). A pneumatic respiration belt and a photoplethysmograph were used for respiration waveform and pulse oximetry measurements, respectively.

The multi-echo EPI data were corrected for time shift, aligned to the first volume of the second echo EPI data (TE=36.6ms), corrected for six-degree rigid motion, spatially smoothed with a 6 mm FWHM Gaussian kernel, and normalized as percentage change. Respiration volume per time (RVT) was derived using the method described by Birn et al. [5]. After correcting the gradient and ballistocardiac artifacts in EEG recorded inside scanner, the band-limited power in alpha frequency band (8-13 Hz) was extracted and averaged across all electrodes, i.e. global field power (GFP). Variations of RVT and GFP were convolved with a respiratory response function [6] and hemodynamic response function [7], respectively, downsampled to the TR, and their correlations with EPI time series of all three echoes were separately calculated. Data from different echoes were then concatenated along the space and subject to the spatial independent component analysis. The time courses of each component were projected and compared to the time course of the RVT and GFP variations.

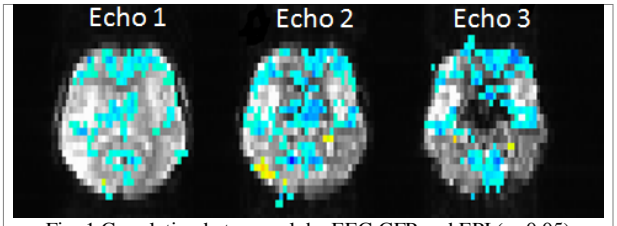

Fig. 1 Correlation between alpha EEG GFP and EPI ($p<0.05$) overlaid on EPIs in three different echo time (14.1/36.6/59.1 ms, respectively)

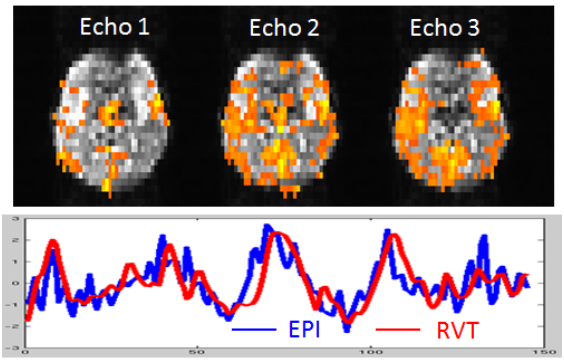

Fig. 2 The independent component analysis of multi-echo EPIs identified a component strongly correlated with RVT variations. Above row shows spatial weights of the RVT-correlated component overlaid on the second echo EPI. Bottom row shows the time courses of RVT and the RVT-correlated multi-echo EPI component

Results and discussion: EPI images of three gradient echoes were reconstructed using the Pruessmann's algorithm [4]. TE-dependent tissue contrasts were observed in images of different echoes. As shown in Fig. 1, negative correlations were found between the global field power (GFP) of alpha-band EEG and EPI time series of three different echoes at eyes-closed condition, mostly in the visual/parietal cortex, medial temporal gyrus, inferior frontal gyrus and inferior parietal lobule. Note that similar yet different spatial patterns of negative correlation were found for EPIs of different TEs, with strongest correlation observed for the 2nd echo (TE = 36.6ms), suggesting that the EEG-related signal originate mostly from the gray matter. Multi-echo EPI data were decomposed into independent components using spatial ICA and a component of strong temporal correlation with RVT variations was identified ($r = 0.65$, $p=0$, plotted in Fig. 2). The spatial weighting of the identified RVT-related IC are distributed across the visual/parietal cortex and medial temporal gyrus, which widely overlap with the areas of EEG correlations and can be significant confounding noise. The weightings are consistently observed across three TEs with increase from short TE to long TE, indicating that the RVT-component are contributed by tissues of long TE property, such as CSF or big vessel flow. Such RVT-component can be removed from the EPI data for denoising.

Conclusion: We have employed a multimodal approach to investigate the physiological noise in BOLD signal. We have shown that multi-echo EPI images can be decomposed into components of neuronal and non-neuronal/physiological origin using the spatial independent component analysis. By comparing with the EEG (alpha GFP) or respiratory variations (RVT), the EPI component of different origins can be identified and denoising can be employed by removing components correlated with physiological variations. Previous studies utilizing single-echo EPI images have explored ICA in separating the physiological noise with limited success, as the spatial distribution of physiological noise overlaps with functioning resting state networks, such as the default mode network [8]. However, this problem is intrinsically overcome in our multimodal multi-echo EPI approach as the neuronally, and physiologically originated signals would have different dynamics across different echoes. Such multimodal multi-echo imaging approach is completely data driven and can be used to further improve resting state fMRI data interpretation.

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