Investigating cardiac pulsatility in the brain using EPI sequences: from physiological noise to physiological information

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Introduction

Resting state fMRI is a popular technique in the study of neural connectivity. Signal fluctuations due to cardiac and respiratory sources, known as physiological noise, are typically filtered or otherwise removed from the fMRI time series[1,2]. Physiological noise may contribute to false positive connectivity[3], and is in general an undesired feature of fMRI data. Cardiac pulsatility is caused by the periodic inflow of blood into brain tissue and intracranial space. One theory posits that the mechanical pulsation in cerebral vessels may provide an index of cerebrovascular health[4]. This mechanical pulsatility is implicated in brain aging and potentially in cerebrovascular pathology like small vessel disease. The purpose of this abstract is to characterize physiological cardiac signal in resting state BOLD fMRI and to compare data from young and elderly participants.

Methods

The cardiac BOLD physiological signal was critically sampled by collecting between 2 and 4 slices sampled at 4Hz. GE-EPI and SE-EPI scans were acquired at a TR of 250ms on a 3T GE scanner. An echo time of 30ms, a flip angle of 34°, and a slice thickness of 5mm were used. The scans were acquired with the following in-plane dimensions: 2x2mm, 128x128 acquisition matrix; 3x3mm, 64x64 matrix; and 4x4mm, 64x64 matrix. 510 time points were acquired per participant. As opposed to whole brain fMRI, a limited number (2-4) of axial slices was chosen to accentuate inflow effects. The slices were centered at the top of the ventricles. The heart rate was recorded using an Invivo MR compatible pulse oximeter. The oximeter was interfaced to a laptop running LabVIEW. High resolution T1 weighted images were acquired for tissue class segmentation, and time of flight scans were acquired to visualize intracranial blood vessels. Data were collected for 9 young controls (22-27 years of age), 3 older controls (62-67 years of age) and 1 transient ischemic attack patient (TIA, 62 years of age). Not all analyses were performed on all subjects because the pulse data was not available for all subjects.

Images were motion corrected, and the first 10 volumes were discarded. Tissue class masks were eroded with a 3mm Gaussian kernel to reduce partial voluming effects and exclude most large blood vessels. The ratio of physiological noise to thermal noise ($\sigma^2_{physio}/\sigma^2_{thermal}$) was compared for different voxel dimensions and pulse sequences (σ^2_{brain}: mean variance in brain, $\sigma^2_{thermal}$: variance of mean background; $\sigma^2_{brain}=\sigma^2_{physio}+\sigma^2_{thermal}$). Power spectra for the 3 tissue classes (CSF, GM, and WM) were determined. A correlation analysis was performed between seed voxels known to exhibit cardiac pulsatility and the rest of the brain. Significance was determined by thresholding at a p value (0.0005) that resulted in minimized background correlation. As an alternate approach, the method of Dagli[5] was used to assign a position in the cardiac cycle ($0\le\theta\le1$) to each EPI volume. The temporal time series were bandpass filtered to allow frequencies ±0.2Hz of the heart rate, and then a Fourier series (Equation 1) was fitted to the intensity as a function of θ (Figure). After this analysis, the percentage of voxels in each tissue class whose intensities significantly depended on θ was determined (Figure 2). Significance was determined by performing an F-test for a nonlinear model ($p<0.01$).

$$f(\theta) = a_0 + \sum_{n=1}^{3} (a_n \cos(n\theta) + b_n \sin(n\theta)).$$

Equation 1. Fourier series.

Results

The ratio of physiological noise to thermal noise ($\sigma^2_{physio}/\sigma^2_{thermal}$) increased with increasing voxel dimensions for all subjects and pulse sequences (Figure 3). This increase was much greater for the GE-EPI sequence than for SE-EPI. The mean tissue class power spectra (not shown) for each subject followed a specific pattern, with peaks at the cardiac frequency, respiratory frequency, and at corresponding harmonics. The CSF showed the greatest amount of cardiac pulsatility in all subjects. A correlation coefficient analysis between voxels in the CSF with significant cardiac pulsatility and the rest of the brain showed differences between the young and elderly controls (Figure 4). Fitting the Fourier series to θ also showed that the tissue class with the most cardiac physiological signal was the CSF (Figures 2, 4).

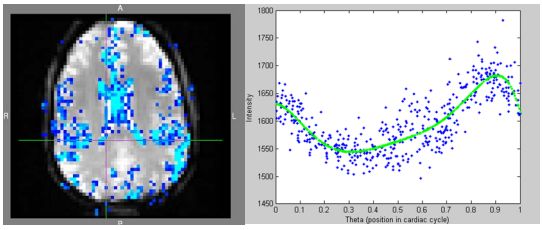

Figure1. A) map of F-values of significantly correlated voxels when using the Fourier series model, B) time course for a sample voxel.

Discussion

The objective of this work was to develop a more thorough understanding of non-neuronal influences in resting BOLD data. Our work adds to recent studies[6] by looking at physiological noise in white matter voxels (Figure 3). The previously studied voxel size and pulse sequence dependences of physiological noise[6] were shown to exist in WM as well as in the whole brain (Figure 3). WM was found to exhibit cardiac BOLD pulsatility despite the fact that WM has lower perfusion levels compared to GM (Figures 2, 4). A significant difference was found between young and elderly participants when measuring the proportion of voxels that showed cardiac pulsatility features (Figure 4). The difference in cardiac pulsatility between the cohorts may be driven by vessel hardening. This is akin to the theory proposed by Moody[4], which states that hardened venules restrict outflow of blood and reflect more of the cardiac waveform into the upstream circulation. Using the Fourier series model[5], all tissue classes showed statistically different percentages of correlation to the cardiac cycle position, i.e. to θ. This result was corroborated by the seed-voxel correlation approach. Our case study involving a TIA patient showed much larger ventricular pulsatility compared to all others (Figure 2). On-going work involves recruitment of individuals with known small vessel disease. The ultimate goal is to attempt to elucidate how age-related changes influence cardiac pulsatility in the brain.

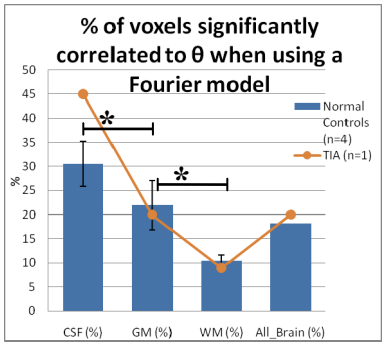

Figure 2. Percent of voxels correlated to cardiac cycle position when using the Fourier series model. (±1 sd, *:NC tissue classes differ at $p<0.05$).

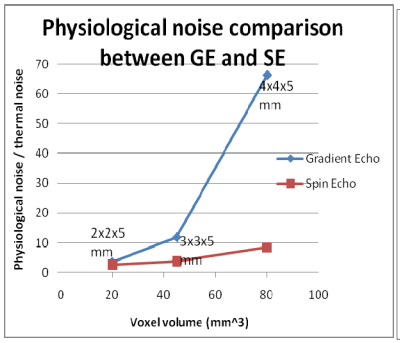

Figure 3. Quantifying voxel dependence of physiological noise for GE-EPI and SE-EPI for a single elderly participant in WM.

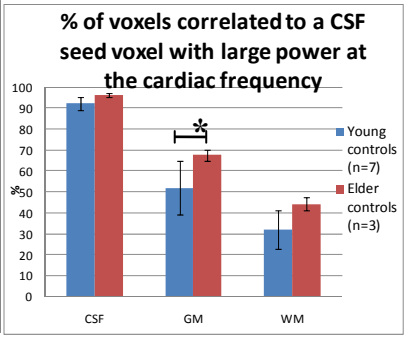

Figure 4. Percent of voxels correlated to a seed voxel in the ventricles when using correlation coefficient analysis. (±1 sd, *: differs from young controls at $p<0.005$)

References [1] Biswal, *MRM*, 1996, 35(1), 107-113 [2] Purdon, *HBM*, 1998, 6(4), 239 -49 [3] Lowe, *Neuroimage*, 1998, 7, 119-132 [4] Moody, *Radiology*, 1995, 194, 469-476 [5] Dagli, *Neuroimage*, 1999, 9(4), 407-15 [6] Yacoub, *Neuroimage*, 2005, 24(3), 738-50