The frequency profile of TE-dependent BOLD physiological fluctuations

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Introduction: Physiological noise, including cardiac pulsations, respiration-related artifacts, fluctuations in arterial CO_2, and spontaneous neuronally induced Blood Oxygen Level Dependent (BOLD) fluctuations changes make it difficult to detect task-dependent activation in fMRI data. Alternatively, the BOLD fluctuations are potentially interesting and effort has been applied to use them to assess connectivity in the brain and to localize "resting-state" networks (1,2,3). Krueger et al. have introduced a model in which physiological noise is divided into BOLD and non-BOLD related components (4). By separating the fluctuations that are echo time (TE) dependent from those that are not TE dependent, they introduced a potential method to cleanly separate BOLD from non-BOLD (and therefore non-neuronal) fluctuations. We investigate this technique further by characterizing the frequency components of the TE dependent and independent signal changes, collected simultaneously using multi-echo EPI acquisition. We found that the TE-dependent BOLD-related physiological fluctuations are primarily at low frequencies, suggesting perhaps spontaneous neuronal activity transduced through the hemodynamic response function. The technique of plotting and mapping the power spectrum of multi-echo-derived time series is useful in separating TE-dependent (susceptibility related) from non TE-dependent (inflow or motion related) signal changes, however the results suggest that several non-neuronally related fluctuations also show a TE dependence.

Methods: Imaging Hardware: 3T General Electric VH/3 MRI scanner (3T/90cm, whole body gradient inset 40mT/m, slew rate 150 T/m/s, whole body RF) equipped with an 8-channel receive coil. Six resting-state runs with varying flip angles were collected using a single-shot multi-echo gradient echo EPI sequence with matrix size 32x32 whilst recording with a respiration belt (n=2). Imaging parameters: Axial plane, 3 slices, FOV/slice 24cm/5mm, TR=350ms, TE=17, 37, 57, 77 and 97ms, flip angles 45, 36, 27, 18, 9 and 0 degrees, number of repetitions=700. TSNR and SNR values were determined voxelwise for the first five flip angle maps with the 0 degree map giving an estimate of the signal independent noise σ_0. By the fitting the equation $TSNR=SNR/\sqrt{(1+\lambda^2 SNR^2)}$ from Krueger et al., the noise contributions of σ_B and σ_{NB} were determined for each of the five echo times. Approximate segmentation masks for gray matter (GM) and white matter (WM) were calculated by thresholding the λ maps using the range of values determined in the Krueger paper. The behaviour of σ_B with respect to echo time was ascertained for GM and WM by averaging over the respective voxels (see Fig 1 for GM example at 5 flip angles). The power spectrum in each voxel was computed for each echo time at a frequency spacing of 0.004Hz. For each frequency, the shape with respect to echo time was correlated with the σ_B TE-dependent shape in both the GM and WM voxels. The resulting timeseries of correlation values was averaged for each segment. The timecourse of respiration volume changes was used in a multiple regression to determine its fit to the data. These maps were thresholded at $p=5x10^{-9}$ and the TE-dependence of those voxels was calculated in a similar manner to above. T_2* and M0 maps where calculated for each timepoint of the original timeseries by fitting $S=M_0 exp(-TE/T_2*)$ to the five TE values using a non-linear fitting algorithm. The power spectra for T_2* and M_0 were calculated and normalized on a voxelwise basis then averaged over GM and WM.

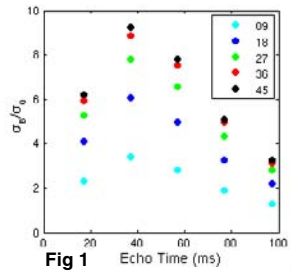

Fig 1

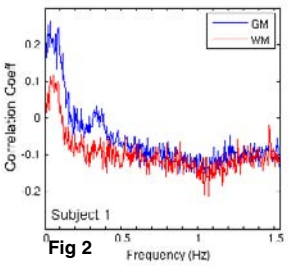

Fig 2

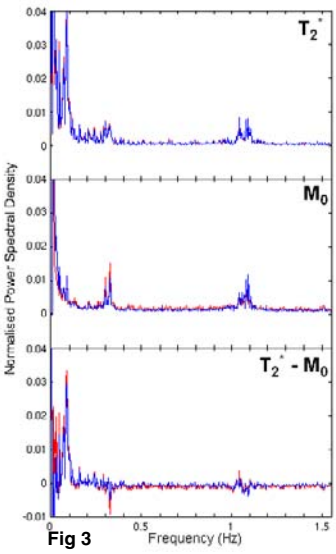

Fig 3

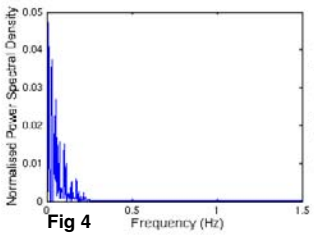

Fig 4

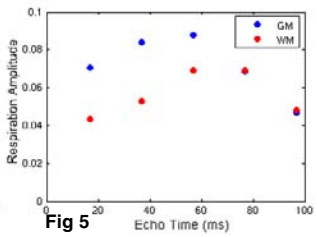

Fig 5

Results and Discussion: The frequency profile of the TE-dependence of BOLD physiological noise is displayed in Fig 2 (averaged over flip angles). Low frequency fluctuations <0.1Hz display the greatest TE-dependence as expected. The higher TE-dependence in GM than in WM around the breathing frequency of 0.35Hz might be related to oxygenation effects that vary over the breathing cycle. There also appears to be a small decrease in TE-dependence around the heart-beat frequency of 1.1Hz. The T_2* and M_0 frequency spectrum and their difference shown in Fig 3 demonstrate that low frequency fluctuations present in T_2* are not evident in M_0. This provides further evidence that the majority of BOLD fluctuations are at low frequencies peaking at approximately 0.1Hz. Resting-state neural activity is inferred from these low-frequency fluctuations. However, there are noise sources in the data that are low-frequency and TE-dependent but not related to neuronal firing. Changes in respiration volume over time are low frequency and peak around 0.03Hz (see Fig 4). The TE-dependence of those voxels that display significant correlation with respiration volume changes is shown in Fig 5. Activation maps based on this TE-dependence correlate well with low frequency TE-dependent maps (0.6). This suggests that there is a significant contribution of this non-neuronal effect to low-frequency physiological fluctuations

Conclusions: By examining multi-echo time series data, TE-dependent physiological noise can be separated from non-TE dependent noise sources. However, not all TE-dependent changes are neuronally related. Therefore, while multi-echo data combined with Fourier analysis is a potentially useful tool for further understanding sources of physiologic fluctuations, it does not completely separate neuronally-related from non-neuronally-related physiologic fluctuations.

References: (1) Biswal et al. 1997, NMR Biomed 10:165-70. (2) Lowe et al. 1998, NeuroImage, 7:119-132. (3) Raichle et al. 2001, PNAS, 98:676 (4) Krueger et al. 1995, Magn. Reson. Med., 46:631-637.