Short TE fMRI data: removing motion and physiological noise confounds from BOLD fMRI

Molly Gallogly Bright[1], and Kevin Murphy[1]
[1]CUBRIC, School of Psychology, Cardiff University, Cardiff, United Kingdom

Introduction: Signal changes in functional MRI data are derived from many sources, including neuronal activation, motion, and physiological changes. The relative contribution of these sources to the fMRI signal is dependent on the echo time (TE) of the signal acquisition. Traditionally, the TE is chosen to optimize blood oxygenation level dependent (BOLD) contrast to identify neuronal sources of signal changes. Short TE data (TE~3ms) does not have robust BOLD contrast, but may reflect many "noise" sources such as head motion [1], spin history effects, motion at the voxel scale (such as cardiac or CSF pulsations), and fluctuations in vascular properties related to arterial gas tensions and respiration. In this study we explore the contribution of these noise sources to signal variance at short TE, as well as the implications of using short TE data to correct BOLD-weighted data, thus improving sensitivity to neuronal activation.

Data acquisition: Ten subjects were scanned using a 3 T GE HDx scanner (Milwaukee, WI, USA). Data were acquired using a dual-echo gradient echo spiral readout sequence (TE1/TE2/TR=3.3/35/2000 ms; 64 spiral; FOV=22 cm; 18 slices; resolution=3.4 x 3.4 x 5.0 mm^3). Four scans were acquired to characterize different contributions to the fMRI signal changes at both echo times:

Rest	Eyes open resting scan	Normal fluctuations
Rest+motion	Eyes open resting scan with additional cued head motion: at ~10 s intervals, a central fixation cross briefly changed color to cue subject to nod their head in a random direction	Amplify head motion
Breathing	Three hypercapnic (breath hold) and three hypocapnic (cued deep breathing) challenges [2] cued using text-based instructions	Amplify physiological changes
Visual	Block design flashing checkerboard (30 s blocks, full contrast, 8 Hz)	Neuronal activation

Respiratory bellows, a pulse oximeter, and gas analyzers connected to a nasal cannula were used to obtain physiological data during all scans. End-tidal O_2, end-tidal CO_2, RVT [3], and cardiac rate [4] data were extracted and interpolated to each fMRI acqusition timepoint. Eight RETROICOR [5] regressors (1^{st} and 2^{nd} order cardiac and respiratory harmonics) were created from the bellows and pulse data. The BOLD-weighted TE2 data were motion corrected (MCFLIRT, FSL, Oxford, UK), and the resulting six translation and rotation regressors were recorded. The visual activation was modeled by a block design paradigm convolved with an HRF.

Data analysis: The motion correction transformations were applied to both TE1 and TE2 datasets to maintain co-registration. The first three volumes were removed, non-brain matter was extracted (BET, FSL), and quadratic detrending was performed (AFNI, NIH, Bethesda, MD, USA). The voxelwise correlation coefficients between the short TE data and the motion, RETROICOR, physiological and visual activation regressors were mapped and thresholded ($p<0.05$, Bonferroni corrected). The BOLD-weighted TE2 data for the **visual** scan were preprocessed in three ways:

Preprocessing 1: Traditional preprocessing: removing the RETROICOR, motion, and physiological regressors;
Preprocessing 2: Traditional preprocessing, additionally regressing out the voxelwise short TE data;
Preprocessing 3: Traditional preprocessing, but *replacing* the motion regressors with the voxelwise short TE data regressors.

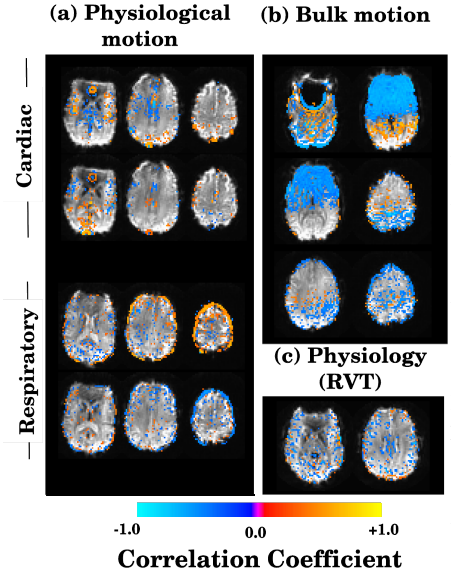

Figure 1. Correlation maps of the **breathing** short TE data and (a) 4 RETROICOR regressors and (c) the RVT regressor, and of the **rest+motion** short TE data and (b) 3 motion regressors. All maps thresholded for significance ($p<0.05$, Bonferroni corrected).

Preprocessing	# voxels	Mean F-stat	Mean F-stat	Mean F-stat
	Main cluster	Main cluster	"OR" mask	"AND" mask
1	58159 ± 19891	39.11 ± 10.16	2.16 ± 0.66	2.16 ± 0.66
2	46564 ± 17861	31.00 ± 6.59	1.77 ± 0.53	1.77 ± 0.53
3	123275 ± 52073	51.89 ± 8.31	4.35 ± 0.93	4.37 ± 0.93

Table 1. The number of voxels and mean F-stat in the main cluster. An "AND" mask and an "OR" mask were created from the main clusters of each preprocessing stream, and mean statistics within these masks are reported. The 3 preprocessing streams were significantly different in all parameters ($p<0.01$, t-test).

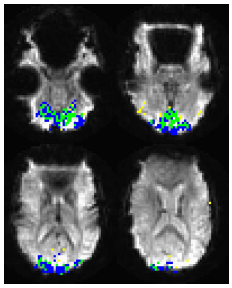

Fig 2. Comparison of the visual activation maps in the short TE (TE1) and traditionally preprocessed BOLD-weighted (TE2) datasets.

The results of each preprocessing stream were analyzed using a GLM and clustering (AFNI) to obtain maps of visual activation. The extent and significance of activation following each preprocessing stream were compared in each subject.

Results: Significant correlation was observed between the short TE (3.3 ms) data and several of the recorded "noise" sources. Fig. 1 shows examples of strictly thresholded correlation maps of individual subjects, illustrating the effect of cardiac pulsation and respiratory motion (RETROICOR), bulk head motion, and RVT on the fMRI signal at short TE. Certain motion parameters (e.g., pitch) were more dominantly correlated with the short TE data than others, which likely reflects the direction in which the subject executed the cued head motion. The short TE data exhibited signal fluctuations correlated with the visual stimulus, which localized to visual cortices. Fig. 2 shows the distributions and overlap of the visual activation maps for the short TE data and BOLD-weighted data (preprocessing 1) for one subject. The extent and significance of the visual activation of the BOLD-weighted data following the three preprocessing streams across 8 subjects (2 subjects removed due to activation not passing clustering thresholds) are summarized in Table 1.

Discussion: Many of the noise sources associated with motion, spin history, cardiac pulsations, and blood volume changes are reflected in the short TE dataset. These results suggest that short TE data, collected simultaneously with BOLD-weighted data in a dual-echo sequence, could be used to correct for these noise sources in BOLD fMRI. However, the short TE data also exhibited signal enhancement associated with the visual stimulus. This phenomenon could be attributable to blood volume changes: previous studies have shown that the short TE "activation" exists in voxels containing large vessels [1] that dilate due to neurovascular coupling. However, there may also be some BOLD contamination at higher spatial frequencies in the latter portion of the spiral readout. Future work is needed to determine whether short TE fMRI directly reflects changes in blood volume, contains moderate levels of BOLD-weighting, or both.

The addition of voxelwise short TE regressors to the preprocessing of the **visual** dataset reduces both the number of activated voxels and mean F-statistic within the activated region (Table 1), possibly indicating that the loss of a degree of freedom is not offset by the gain in noise removal. However, the use of voxelwise short TE data regressors *in lieu* of motion regressors significantly increases the extent and significance of the activation maps. Closer inspection revealed that one or more of the motion regressors were highly correlated with the visual stimulus (possibly an artifact of intensity-based registration or task-correlated motion), and thus these regressors removed much of the "activation" variance in the BOLD-weighted data. The use of the short TE regressors ameliorated much of this problem in all subjects. In conclusion, short TE data can be acquired simultaneously with BOLD fMRI data without affecting scan duration and may be helpful in noise correction, particularly in clinical populations where motion and physiological fluctuations are likely to be amplified.

[1] Buur NMR Biomed (2009) 22; [2] Bright NeuroImage (2009) 48; [3] Birn NeuroImage (2006) 31; [4] Shmueli NeuroImage (2007) 38; [5] Glover MRM (2000) 44