A statistical method for computing BOLD activations in multi-echo time fMRI data sets and identifying likely non-BOLD task related signal change

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Introduction

Multi-echo time echo planar image acquisitions allow for the consideration of BOLD related T_2* decay. Studies which have included single-shot, multi-echo acquisitions to calculate T_2* have been shown to yield activations which are appropriately localized when compared to proton spin density images calculated from the same T_2* weighted images (1), allowing the separation of BOLD T_2* effects from other effects which arise in the proton spin density images. However, such pulse sequences require the acquisition of additional data in each shot, reducing the available slice coverage for a given TR. In this abstract, we present a method for the statistical analysis of multi-echo time fMRI data, and apply it to data acquired in a pulse sequence where the echo time is shifted by 20 ms for alternating TRs, thereby allowing the same slice coverage as standard, single echo data acquisitions.

Theory

BOLD contrast relies upon a change in the T_2* decay rate of blood as oxygenation changes during cortical activation. Previous studies have found that the T_2* of blood changes from 45.33 ms in rest to 46.56 ms during task at 3.0 T (2). Thus, different BOLD contrast is expected with different echo times, as seen in Figure 1. True BOLD activations are expected to exhibit changes in BOLD contrast that corresponds to this theoretical result, while other potentially task related signal not of interest may exhibit a different echo-time-dependent contrast pattern.

A general linear model was developed to be applied to multi-echo time data. For the case of two echo times, the model includes a six column design matrix X, including one column for the baseline signal of the first echo time (TE_1), one column for the baseline signal of the second echo time (TE_2), one column for the centered linear trend of TE_1 data, one column for the centered linear trend of TE_2 data, one column for the task related response to TE_1, and one column for the task related response to TE_2. The voxel-wise model is shown in Equation 1, where n is the number of time points, y is a vector of the observed time series, β is a vector of unknown regression coefficients, and ε is a vector of normally distributed noise ($\varepsilon \sim N(0, \sigma^2 I_n)$).

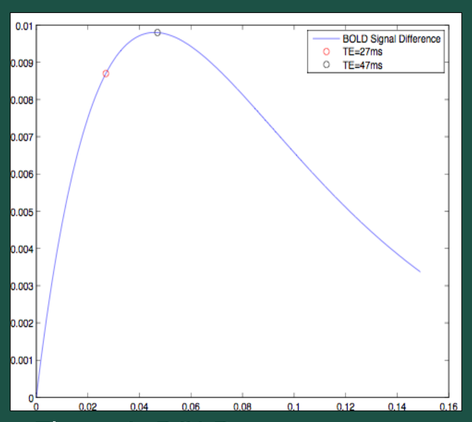

Figure 1. BOLD response curve

Analysis

Functional neuroimages were acquired in a subject, in concordance with the procedures of the institutional review board. The subject performed a visually-cued block-designed bilateral finger-tapping task with 7 epochs of 16 seconds rest, 16 seconds task, followed by 16 seconds of rest. Scanning parameters included TE_1=47.0 ms, TE_2=27.0 ms, TR=2 s, flip angle=90 degrees, acquisition matrix=64×64, field of view=24 cm, slice thickness=5 mm, 8 channel head receiver on a 3.0 T General Electric Signa LX imager. Activations were computed to find voxels active in only TE_1 data, only TE_2 data, and both TE_1 and TE_2 data. Chi-squared statistics were computed from the model through a likelihood ratio test, and were thresholded with an α=0.05, Bonferroni adjusted threshold. Contrasts of C_1=(0 0 0 0 0 1), C_2=(0 0 0 0 1 0), and C_3=(0 0 0 0 1 1) were utilized to determine voxels which were active in the data acquired with the second echo time, first echo time, and either echo time, respectively.

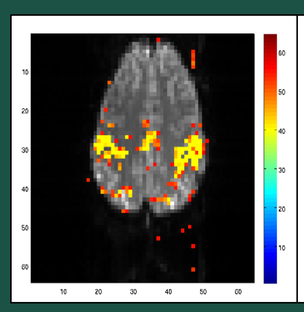

Figure 2. C_1 Active

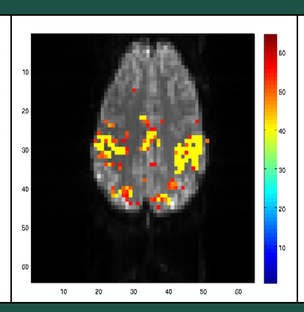

Figure 3. C_2 Active

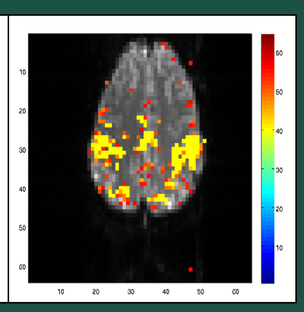

Figure 4. C_3 Active

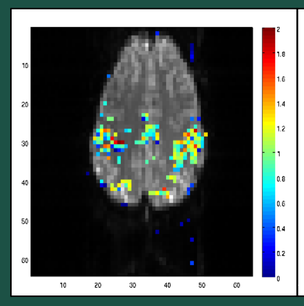

Figure 5. C_1, β_5/ β_6

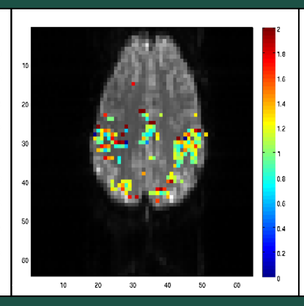

Figure 6. C_2, β_5/ β_6

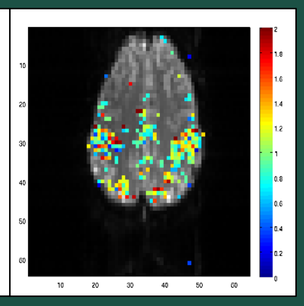

Figure 7. C_3, β_5/ β_6

$$\begin{bmatrix} y_1 \\ y_2 \\ y_3 \\ y_4 \\ y_5 \\ y_6 \\ \vdots \\ y_{n-1} \\ y_n \end{bmatrix} = \begin{bmatrix} 1 & 0 & -n/2 & 0 & -1 & 0 \\ 0 & 1 & 0 & -n/2 & 0 & -1 \\ 1 & 0 & -n/2+1 & 0 & -1 & 0 \\ 0 & 1 & 0 & -n/2+1 & 0 & -1 \\ 1 & 0 & -n/2+2 & 0 & 1 & 0 \\ 0 & 1 & 0 & -n/2+2 & 0 & 1 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 1 & 0 & n/2 & 0 & -1 & 0 \\ 0 & 1 & 0 & n/2 & 0 & -1 \end{bmatrix} \begin{bmatrix} \beta_1 \\ \beta_2 \\ \beta_3 \\ \beta_4 \\ \beta_5 \\ \beta_6 \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \varepsilon_3 \\ \varepsilon_4 \\ \varepsilon_5 \\ \varepsilon_6 \\ \vdots \\ \varepsilon_{n-1} \\ \varepsilon_n \end{bmatrix}$$

$$y = X\beta + \varepsilon$$

Equation 1: Multi-TE Model

Results

Activations found with contrasts C_1, C_2, and C_3 for a representative slice are shown in Figures 2, 3 and 4. The different echo times are sensitive to different voxels, with the longer echo time yielding more activations with its increased T_2* weighting, and the case C_3 of considering both echo times simultaneously yielding the most activations. To consider the T_2* dependence of the observed activations, the ratio of β_5 to β_6 is shown for the active voxels with constraints C_1, C_2, and C_3 for the same slice in Figures 5, 6 and 7. As indicated in Figure 1, the expected BOLD response should yield a ratio of about 1.15.

Discussion

The ratio of task related functional responses to different echo times can be used to identify voxels which exhibit expected functional BOLD contrast. In support of this methodology, Figures 5 and 7 illustrate that clear false positives outside of the brain can be excluded as the ratio is much less than one, while the expected BOLD ratio is slightly greater than one. Additionally, voxels on the periphery of activated regions exhibit TE dependent ratios which are markedly different from the expected BOLD ratio, suggesting that these voxels may be exhibiting a task related contrast which differs from the expected BOLD contrast, perhaps associated with varying partial volume effects from task related motion.

References

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2. Lu, H., and van Zijl, P. C.M. Magnetic Resonance in Medicne 53, 2005: 808-816.

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