Determination of Onset Latencies Using Coherence Analysis in fMRI

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Introduction

At present, most fMRI analysis methods depend on the temporal characteristics of blood oxygenation level dependent (BOLD) signals. However, due to the variability of hemodynamic response function [1] and the low-frequency physiologic noises, [2] the statistic power to detect the activated voxels may be decreased. In contrast, coherence analysis measures the similarity in frequency domain and can detect activated areas associated with rhythmic stimuli irrespective of the time lag. The calculated phase lag can be represented as the relative onset time of BOLD response between regions and provides detailed temporal information in fMRI. Here, we examine the sensitivity of coherence analysis at the first step and then validate the capability of retrieving the phase lag by coherence analysis using hemi-visual field stimulation with varying delay time

Methods

Two normal right-handed volunteers in late twenties participated in the fMRI experiment. All scans were done on 3T Bruker Medspec scanner (Ettlingen, Germany) with the following parameters: GE-EPI with TR/TE:2000/33 ms, flip angle: 77, FOV: 30cm, 128*128 matrix. Slice orientation was 8 axial slices parallel to AC-PC line with thickness 3mm and gap 0.75 mm to cover the visual cortex.

Visual stimuli with 8 Hz flickering checkerboard in hemi-visual fields was given to both eyes of subjects by an LCD goggle. The stimulation duration was 2 sec followed by fixation. Left side stimulus comes first. The phase lag between left and right was set to be 0° to 180°, step 30° in the first stage of experiments and later set to be 0° to 25°, step 5°in the second stage. The trial length is 30 sec; therefore 5° phase lag equals 416.7 ms time lag. Eight trials were given for each phase lag. With the initial wait of 16 sec, the total scan time is equal to 256 sec.

The fMRI data was preprocessed by SPM2 (FIL, UCL, London, UK). Realignment, slice-timing correction, and smoothness (FWHM=5mm) were performed in the preprocess. Then the fMRI data were analyzed by the coherence method using the stimulus paradigm as the reference function. Brain voxels showing high coherence (coh > 0.85) with the reference function at the stimulus-presenting frequency (in our study: 1/30 Hz) were marked as activated. To overcome the limitation of small sample size in fMRI time course, we utilize the multi-taper method for spectral estimation. [3]

For data $x(n), y(n)$, and K orthonormal tapers $w_k(n)$, let the K^{th} estimator $\hat{R}_{k,x}(e^{jw})$ is defined as:

$$\hat{R}_{k,x}(e^{jw}) = \frac{1}{N}\left|\sum_{n=0}^{N-1} w_k(n)x(n)e^{-jwn}\right|^2$$

Then the simple averaged multitaper (MT) spectral estimator is defined as

$$\hat{R}_x^{(MT)}(e^{jw}) = \frac{1}{K}\sum_{k=0}^{K-1}\hat{R}_{k,x}(e^{jw})$$

$\hat{R}_{xx}^{(MT)}, \hat{R}_{yy}^{(MT)}, \hat{R}_{xy}^{(MT)}$ are estimates of the power spectrum of x,y and the cross-spectrum. Coherence is $Coh_{xy} = \frac{\left|\hat{R}_{xy}^{(MT)}\right|^2}{\hat{R}_{xx}^{(MT)}\hat{R}_{yy}^{(MT)}}$, and phase: $\Phi_{xy} = \tan^{-1}\left(\frac{\operatorname{Im}\hat{R}_{xy}^{(MT)}}{\operatorname{Re}\hat{R}_{xy}^{(MT)}}\right)$

The tapers are chosen to minimize spectral leakage outside a given bandwidth. One optimal set is the discrete prolate spheroidal sequences (DPSS, also known as Slepian sequences). [3] For comparison, we also performed correlation analysis with correlation threshold >0.5.

Results

In both stages of hemi-visual field stimulation, coherence analysis can clearly identify bilateral visual cortices, even though the phase lag is large. In contrast, correlation analysis under conditions with larger phase lag could only detect right hemisphere activations; part of the left visual cortex was even marked as negatively correlated. (Fig.1) We calculated the mean phase in bilateral visual cortices and plot the phase lag between the two sides (left minus right) against the stimulus onset lags. (Fig.2) The calculated phase lags in visual cortices was highly correlated with the stimulus lags (R^2=0.9634,0.9805). However during smaller phase lags(0°~25°), coherence tends to underestimate the phase lag (regression coefficient=0.6284).

Discussion

Our study demonstrated the feasibility of coherence analysis in fMRI study despite the time lag. This is in contrast with the convention temporal domain method, such as correlation study. We also show that the temporal information can be estimated with the calculated phase, which in conventional studies is obtained by rapid sampling (short TR) and averaged time course. [4] With short TR, the slice coverage is usually limited.

Yet there are also limitations in coherence analysis. First the stimulus must be rhythmic. Second, there is large variance in estimated phases for voxels in a given ROI. The reason may be statistical error or the variability of the hemodynamic response for each voxel in the ROI.

References:

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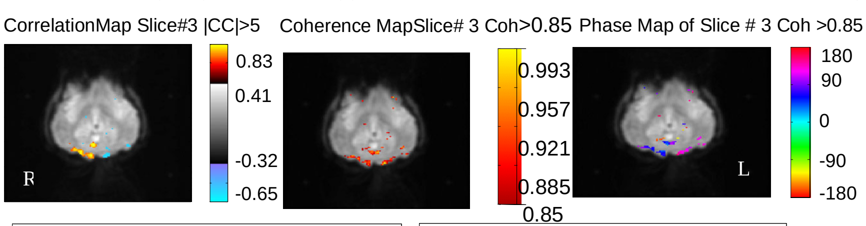

Fig.1 , Correlation map *(left)*, coherence map *(middle)*, and phase map *(right)* in study with stimulus phase lag of 90°. Correlation marked the left visual cortex as negatively correlated. Coherence could clearly detect bilateral activation. The phase in the left visual cortex is 90° later than that in the right side, compatible with the stimulus onset lags.

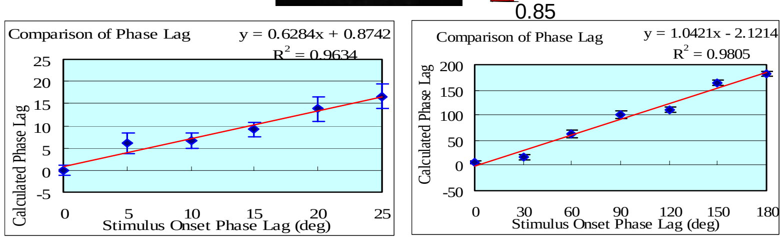

Fig. 2, Comparison of phase lag between bilateral visual cortices and stimulus onset in smaller (0°~25°) (*left*) and larger (30°~180°) (*right*) lags. At large phase lag (>30°), there is precise correlation between the calculated lag and the stimulus onset lag. At smaller phase lag, our method tends to underestimate the phase lag. Error bar represents the 95% confident interval.