Baseline BOLD Correlation Accounts for Inter-Subject Variability in Task-Evoked BOLD Responses

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Introduction Spontaneous blood-oxygen-level-dependent (BOLD) fluctuations under the resting brain state have been widely observed and hypothesized to reflect the ongoing activity of the brain. An interesting question about such ongoing activity is *if* and *how* (if yes) it would affect task-evoked brain activity [1] which can be studied by fMRI (functional Magnetic Resonance Imaging) BOLD contrast. The purpose of the present study is to investigate the relation between spontaneous BOLD fluctuations and evoked BOLD responses. To do this, BOLD signals were acquired from the human visual cortex under the conditions with/without visual stimulation. Correlation strength and fluctuation magnitude of baseline BOLD signals were quantified and correlated to amplitude of evoked BOLD responses. The group-based analysis was used instead of the individual-based analysis, because it is important to utilize the large inter-subject variability to increase the dynamic range of evoked BOLD responses.

Methods Fourteen healthy subjects were scanned on a 4T/90 cm bore magnet (Oxford, UK) system with the Varian INOVA console (Varian Inc., Palo Alto, CA). Seven consecutive gradient-echo planar image (GE-EPI; coronal) slices covering primary visual cortex were acquired (FOV = 20×20 cm^2; TR/TE = 1100/30 ms; 64×64 matrix size; 5 mm thickness) with the experimental paradigm using a full-field reversal checkerboard visual stimulus (Fig. 1). The data were acquired 4 to 7 runs (300 image volumes or 5.5 minutes per run) for each subject; and each run was divided into the baseline (eyes fixed on a white cross; Fig.1, red shadow) and stimulation (Fig. 1, green shadow) stages. The baseline stage was used for calculating the reference BOLD level (100%). The stimulation stage was used to create a functional activation map (the correlation map with respect to the experimental paradigm), and a region of interest (ROI) was defined to cover the most activated ~350 pixels. Within the ROI, the amplitude of evoked BOLD responses was quantified at evoked BOLD plateaus (Fig. 1, blue shadow), the fluctuation magnitude of baseline BOLD was estimated through the standard deviation of the baseline signals, and the correlation strength of baseline BOLD fluctuation was calculated by averaging correlation coefficients between each pair of pixels. A correlation map with respect to the most activated pixels was also created for the baseline stage to examine the spatiotemporal correlations of baseline BOLD signals. In addition to the correlation analysis, the independent component analysis (ICA) was also performed for the date of the baseline and stimulation stages to extract the meaningful components.

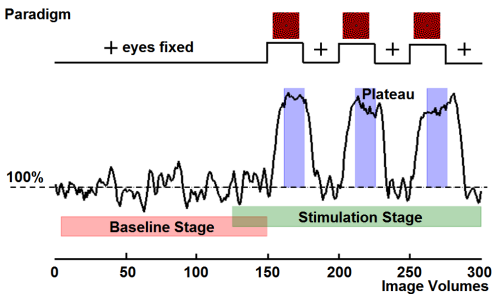

Fig. 1 Experimental paradigm and general strategy for processing data.

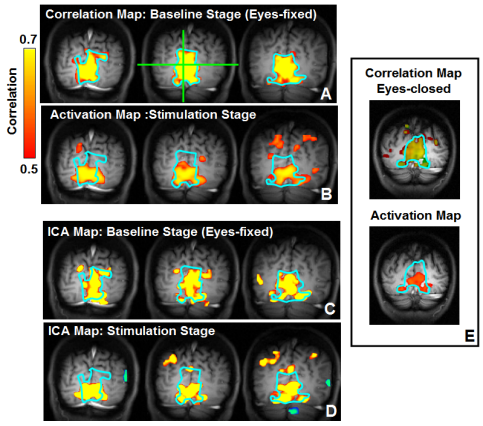

Fig. 2 Correlation map (A), activation map (B), and ICA maps (C and D) from a representative subject are compared with the maps obtain previously (E).

Results Correlation map for the baseline stage (eyes-fixed condition) and functional activation map for the stimulation stage from a representative subject are shown in Figs. 2A and 2B. Compared to the activation map, the correlation map covers wider brain regions; and their major difference is in the *cuneus gyrus* region. The result is also consistent with the maps in Figs. 2C and 2D based on the ICA analysis. This observation is similar with the difference previously found between the baseline BOLD correlation map under eyes-closed condition and the activation map obtained with same full-field visual stimulation [2] (Fig. 2E). This may suggest that the spatiotemporal correlation pattern of spontaneous BOLD signals will not change significantly under eyes-closed and eyes-fixed conditions.

The correlation strength and fluctuation magnitude of baseline BOLD and the amplitude of evoked BOLD within the ROI were calculated for all the subjects and summarized in Fig. 3. A strong positive correlation (R^2 = 0.68, *p*-value = 2.3 × 10^{-4}) was found between the correlation strength of baseline BOLD and the amplitude of evoked BOLD. However, the correlation between the fluctuation magnitude of baseline BOLD and the amplitude of evoked BOLD did not reach a significance level in the present study (R^2 = 0.02, *p*-value = 0.64).

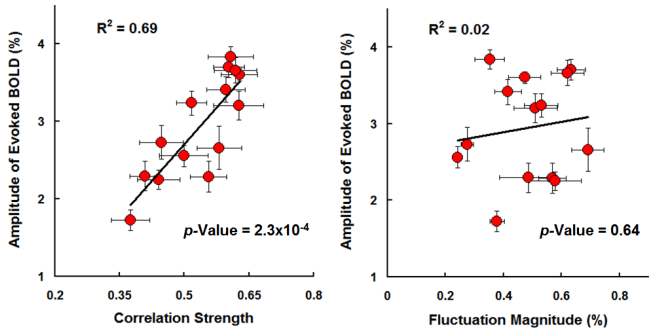

Fig. 3 Scatter plots of individual data and linear regression lines, showing the correlation of task-evoked BOLD amplitude versus correlation strength (left panel) and fluctuation magnitude (right panel) of baseline BOLD. Error bars represent standard error across different runs for the same subject.

Discussion In this human study, we found that correlation but not magnitude of spontaneous BOLD fluctuations accounts for inter-subject variability in the amplitude of task-evoked BOLD responses. This finding may suggest that synchronization strength of ongoing brain activity has an important effect on evoked brain activity, even at the early stage of sensory systems. It indicates a tight correlation between the baseline state and the functional outcome of brain activation. This notion is consistent in some extent with previous studies [3-4], showing that human behavior/perception could be affected by the magnitude of spontaneous BOLD fluctuations (though not clear in regards to correlations in those studies). Our finding also indicates that large inter-subject BOLD variability in response to the same stimulation commonly seen in many fMRI applications could attribute to the varied brain baseline state which could be measured noninvasively by the correlation strength of ongoing BOLD fluctuation.

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References [1] Friston KJ. et al. *Science* 2009; [2] Liu X. et al. *ISMRM* 2008, p2412; [3] Fox MD. et al. *Neuron* 2007 ; [4] Hesselmann G. et al. *PNAS* 2008.