Spatial and Temporal Characteristics of Evoked and Induced Neural and Vascular Responses Assessed with Simultaneous EEG-fMRI

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Introduction

Neural responses to stimuli consist of two components: one represents the evoked response that is specific to stimulus content and thus directly related to the stimulus processing; the other is the induced response that is non-specific or less specific to stimulus content and may reflect the change of spontaneous activity as an indirect effect of the stimulus. Separating these two would help address the interaction of baseline spontaneous activity and stimulus evoked activity, although this may be very difficult to achieve with blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI) alone. In the present study, we simultaneously acquired electroencephalography (EEG) and fMRI data while visual stimuli were presented at a specific temporal frequency. Such frequency specificity allowed us to effectively tag the evoked neural response with the stimulus frequency (SF) so that the change of EEG power at SF could be used to extract the evoked response. To assess the spontaneous activity, we focused on the power fluctuation in the alpha band (8-12 Hz), which is a dominant frequency feature of spontaneous EEG. With this frequency-tagging technique, we investigated the contribution of the evoked (SF) and induced (alpha) EEG responses to BOLD-fMRI. Special attention was paid to the partial correlation between the BOLD signal and the alpha power fluctuation as well as its implication for the temporal and spatial characteristics of the BOLD response.

Methods

From four healthy volunteers, we acquired concurrent EEG (32-channel, BrainProducts) and BOLD fMRI (GRE-EPI, rate-2 SENSE, TE/TR=30ms/1.5s, 30 4mm axial slices, FOV=220×165mm^2, matrix size=64×48) using a GE 3T Signa scanner equipped with a 16-channel receive-only coil array. Each subject was first instructed to rest with multiple cycles of self-paced alternating eyes-closed and eyes-open periods of about 30 sec each, and then performed a fixation task while a contrast-reversal visual stimulus (full-field, black-and-white contrast, reversal frequency of 5.95 Hz) was presented using a block design with three 30s stimulus-on blocks interleaved with 30s stimulus-off blocks). Based on the eyes-closed-eyes-open task, the individual alpha frequency (IAF) was determined as the frequency within the alpha band (8-12Hz) that gave the maximal EEG spectral difference at the occipital electrodes between eyes-closed and eyes-open periods. For the visual paradigms, we computed the EEG spectrogram (i.e. power as a function of time and frequency) by spectral estimation with a 2s window sliding in 1s steps, and extracted the power fluctuations at SF and IAF based on the occipital electrodes. We then applied a general linear model (GLM) analysis to the BOLD-fMRI data by using two regressors derived from the SF and IAF power fluctuations convolved with a canonical hemodynamic impulse response function (HRF). Results were compared to those of conventional GLM analysis in which a task regressor was derived from the stimulus boxcar convolved with HRF.

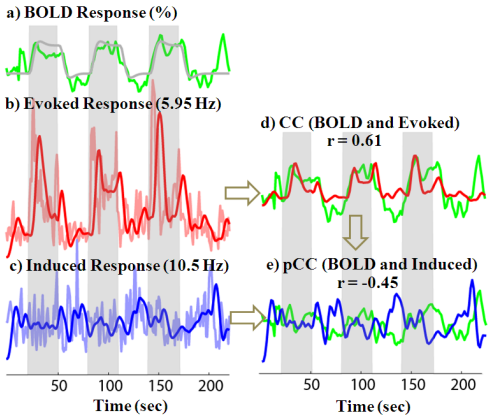

Figure 1. a) Average BOLD signal (green) in visual cortex and stimulus boxcar-derived regressor (gray), b) SF-tagged EEG power fluctuation (light red) and its derived regressor (red), c) IAF-tagged EEG power fluctuation (light blue) and its derived regressor (blue). Right column illustrates the level of correlation between BOLD and SF-regressor (d) and the partial correlation between IAF-regressor and SF-regressor (e).

Results

Figures 1 and 2 show the results from a single subject. In the visual cortex, the 30s stimuli gave rise to BOLD signal increase (Fig. 1.a), EEG power increase at the stimulus reversal frequency (Fig. 1.b), and EEG power decrease at the alpha frequency (Fig. 1.c). The time course of induced response (i.e. IAF-power decrease) was much less specific at the stimulus onset and offset than those of the BOLD and evoked responses (i.e. SF-power increase). The SF-power was strongly and positively correlated with the BOLD signal, whereas a negative partial correlation also existed between BOLD and IAF-power. Across subjects, the partial correlation (mean ± standard error) between BOLD and induced IAF-power was −0.29±0.05; the partial correlation between BOLD and evoked SF-power was 0.68±0.04. Combining both SF-power and IAF-power in a GLM analysis, we found that the BOLD response positively driven by the evoked SF-power increase was confined to the visual cortex (Fig. 2.b), whereas the BOLD response negatively driven by the induced IAF-power decrease was more extended beyond the visual cortex and into the parietal cortex (Fig. 2.c). In comparison, the conventional GLM analysis based on the stimulus boxcar-derived regressor led to an activation map that overlapped with BOLD correlates of both the evoked and induced EEG responses (Fig. 2.a). Maps obtained from three other subjects were generally comparable, whereas some positive BOLD correlates to IAF-power were found at frontal cortex for one subject and at the regions of the default-model network for another subject.

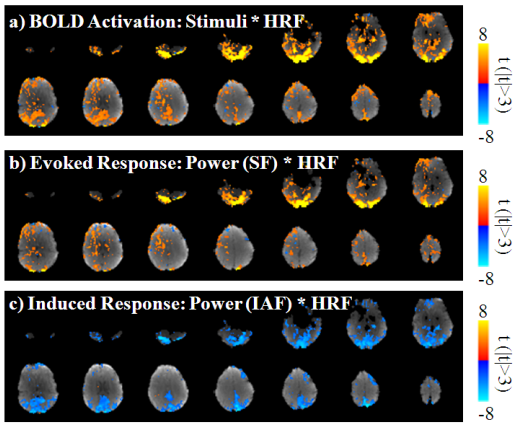

Figure 2. Statistical parametric maps (|t|>3) associated with three different regressors derived from stimulus boxcar (a), SF-power (b) and IAF-power (c).

Discussion

The BOLD response to visual stimulation arises from a combination of evoked and induced neural activity. Using simultaneous EEG-fMRI and frequency-tagging techniques, we were able to separate these distinct neural components and to investigate their corresponding temporal and spatial characteristics in terms of both EEG and fMRI. The time course of the evoked response had a very specific change in relation to stimulus onset and offset, whereas the induced response was less specific, but not entirely non-specific. Spatially, the evoked response was confined to the areas known to be directly involved with the stimulus processing, whereas the induced response covered more extended regions. These findings have important implications for the quantitative interpretation of BOLD-fMRI. It suggests that both the spatial extent and amplitude may be over-estimated in a normal stimulus-versus-rest fMRI experiment, which measures the sum of the evoked and induced components.