On the Cross-Modal Relationship Between fMRI and EEG

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Introduction Functional magnetic resonance imaging (fMRI) often uses the blood oxygen level dependent (BOLD) signal as a surrogate index of neural activity. The coupling between neural and BOLD signals is commonly modeled as a linear time-invariant system, which serves as an approximation for the complex interactions between neuronal activity, metabolic demand, blood flow and oxygenation[1]. However, the linearity of the neurovascular coupling has been the subject of a vast number of studies, in which electrophysiological and hemodynamic signals are individually quantified before being compared against a linear function. The variety of ways for quantifying multimodal signals has confounded the interpretation of previous findings reported in the literature, and may partly account for the existing disagreements on the linearity of the neurovascular coupling. In the present study, we modeled the cascaded interactions between stimuli and neural and vascular responses, and proposed a pair of quantitative measures for assessing the relationship between electrophysiological and hemodynamic signals. The neurovascular coupling in the human primary visual cortex was investigated through visual stimulation experiments using a variable visual contrast.

Modeling As illustrated in Figure 1, external stimuli induce the BOLD signal change sequentially through two systems representing neural and hemodynamic impulse responses, respectively. The neural impulse response function (NRF) represents the electrophysiological response to an impulse stimulus. Our previous study has demonstrated that the neural response evoked by sustained and repetitive stimuli can be represented by convolving the stimuli (modeled as a train of delta functions) with the NRF, given that the inter-stimulus interval (ISI) is longer than 200 ms so that the neural refractory effect is negligible. The hemodynamic impulse response function (HRF) represents the hemodynamic consequence of a neural impulse signal. A linear neurovascular coupling implies that the vascular response can be represented by convolving the neural response with the HRF. However, our previous study has identified the vascular nonlinearity originating from the vascular refractory effect, which manifests itself as the over-prediction by the linear HRF when the ISI is shorter than 4 sec. Since such a nonlinear effect is independent of the absolute BOLD response level, it can be taken into account by using a refractory turning curve (RTC) defined as a piece-wise linear function of ISI. According to our previous theoretical modeling study[2], the system as shown in Fig. 1 also implies that the integrated power of neural impulse response is proportional to the BOLD effect size, which is computed as the ratio between the measured BOLD signal and a predictor derived from the stimuli, the HRF and the RTC curve.

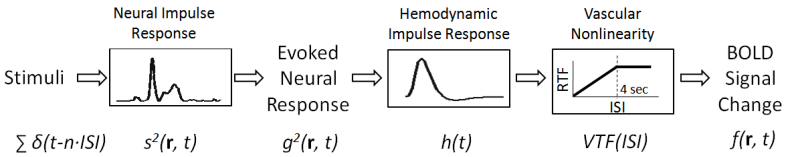

Figure 1 A system model describing the cascaded processes from stimuli to BOLD signals.

Experiment To test the above model, 10 subjects were presented with a lower-right quarter-circular grating visual pattern reversing at 2 Hz with variable contrast (5, 10, 20, 40, 60, 80 and 100%). EEG (64 channel, BrainProducts, Germany) and fMRI (3T Siemens Trio scanner, Germany) signals were acquired simultaneously from 5/10 subjects and separately from the other 5/10 subjects. Each subject underwent at least four sessions. Within each session, the stimuli were presented in a block-design manner. Seven 30-sec blocks with sustained stimuli of varying contrast were interleaved with eight 30-sec resting blocks. Visual evoked potentials (VEP) were obtained through averaging over >240 trials of the same visual contrast. FMRI activation maps were derived by using the general linear model (GLM) based analysis (BrainVoyager QX, Brain Innovation, Germany). The BOLD effect size for a region of interest (ROI) within the left primary visual cortex (V1) was computed as aforementioned. An fMRI-seeded dipole fitting analysis was performed with five fixed current dipole sources (BESA, MEGIS GmbH, Germany). The dipole locations were fixed to the centers of the fMRI activations in the left V1 and four bilateral extrastriate areas, respectively. The dipole time courses were estimated by fitting the dipole moments with the VEP signals. The power of the estimated dipole moment was integrated during an "event-related" time window from 0 to 500 ms following the stimulus onset. Linearity was assessed for the relationship between the integrated dipole source power and the BOLD effect size in the left V1.

Results Figure 2 shows the results averaged across 10 subjects. The BOLD signals and the dipole time courses in the left V1 and the VEP signals at the Oz channel all exhibited gradually higher amplitudes in response to presentation of stimuli with increasing contrast. The relationship between the BOLD effect size and the integrated current source power in the left V1 was well represented by a linear function (r=0.99) after the correction of RTC, in agreement with our theoretical modeling prediction. The integrated current source magnitude was relatively less correlated with the BOLD effect size (r=0.90) (data not shown herein).

Conclusion Our modeling study suggests a linear relationship between the BOLD effect size and the integrated power of the neural impulse response (or the event-related current source signal). This is regardless of the presence of the vascular nonlinearity attributed to the vascular refractory effect, since this nonlinear effect can be compensated and corrected by using the RTC. This theoretical result is well supported by the present experimental data, which indicate that the BOLD effect strongly correlates with the integrated current source power at V1 in response to visual stimuli with variable contrasts. The fact that the integrated current source power correlates better with the BOLD effect size than the integrated current source magnitude may suggest that the power of neural activity is the physical correlates of metabolic energy driving the vascular response measured by fMRI. We also recommend the use of the BOLD effect size and the integrated power of the event-related neural activity as a pair of "matched" measures, theoretically driven by a well-defined modeling hypothesis, for assessing the linearity (or nonlinearity) of the neurovascular coupling. Furthermore, the present conclusion with regard to the fMRI-EEG cross-modal relationship leads to a solid theoretical basis for recent and future methodological developments in attempt to integrate fMRI and EEG (or MEG) as a combined multimodal neuroimaging technique[2]. Such integration holds great potential to offer uniquely high spatiotemporal resolution by utilizing the complementary while closely coupled features of both modalities.

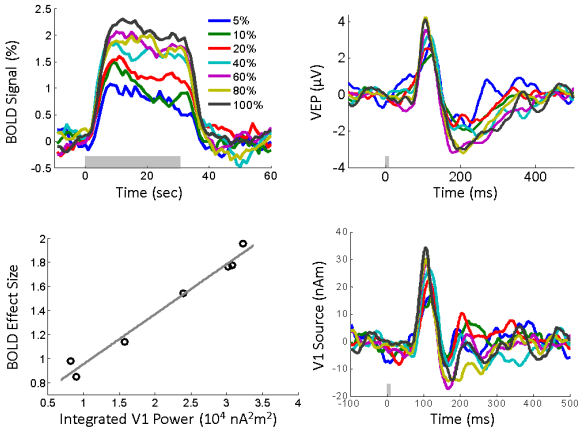

Figure 2 (Upper-Left) BOLD signals at the left V1; (Upper-Right) VEP at the Oz channel; (Lower-Right) Current dipole time courses at the left V1; (Lower-Left) BOLD effect size at the V1 ROI vs. the integrated V1 current source power.

References 1. *Heeger & Ress, Nat. Rev. Neurosci. 2002*; 2. *Liu & He, NeuroImage, 2008.*

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