Hemodynamic Responses to Transient Brain Deactivations: Modifications to the Balloon Model to Account for Non-linear Effects

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Introduction:

FMRI based on the blood oxygenation level-dependent (BOLD) effect usually relies on measuring MR signal changes caused by increases in blood oxygenation, flow and metabolic activity. In event-related designs, the hemodynamic response function (HRF) characterizes the response of the MRI signal to a transient stimulus. Much less attention has been paid to deactivations, the signal decreases observed in many studies following a change in conditions. In particular, analyses of fMRI data usually assume that the HRF for signal decreases is the same as for signal increases, and that BOLD signals superimpose linearly in practical applications. In this study, we investigated the spatial and temporal patterns of negative BOLD effects for transient decreases in stimulation in visual cortex. The study was designed to characterize better the negative BOLD responses evoked by event-related decreases in neural activation. We elicited negative BOLD responses by using a visual event-related paradigm in which we switched off a stimulus for a short time during otherwise continuous sustained stimulations. The HRF for deactivation is clearly not the inverse of the HRF for activation.

Method:

An 8Hz large-field contrast-reversing checkerboard pattern at 100% contrast served as a visual stimulus (denoted as condition “ON”) and a spatially uniform black screen served as a second condition (denoted as condition “OFF”). Event-related paradigms generated by E-prime (Psychology Software Tools, Inc) were presented to subjects in an fMRi scanner. Various durations of visual inactivity (stimulus “OFF” for 1sec, 2sec, 3sec, 4sec, 6sec, or 8sec) were interspersed during otherwise continuous visual stimulation (“ON”) to assess the effects on BOLD signals and test for signal linearity. A total of 8 scanning runs were acquired, each run started with a 22s flashing checkerboard steady state period follow by the variable durations of stimulus-OFF.

MR images were acquired on a 3T Philips Achieva scanner. Ten T1-weighted anatomic images were collected parallel to the AC-PC line with 5mm slice thickness and 1mm gap and positioned to cover the visual areas. Then functional images were collected in the same planes, using a gradient echo EPI sequence (TR/TE=1s/35ms, flip angle=70^o, FOV=22x22cm^2 and acquisition matrix size=80x80 reconstructed to 128x128), then analyzed using BrainVoyager and programs running under MATLAB.

Results:

The MR signal in primary visual area V1 showed a transient negative response to brief periods of stimulus OFF (Figure1). The response was different in amplitude and extent for different durations of stimulus OFF. To quantify differences between responses, we fit the experimental signal decreases with a modified gamma-variate function $f = (t/d)^a e^{-(t-d)/b} - c(t/d')^{a'} e^{-(t-d')/b'} + E$ in the least-squares sense (Liao, 2002) to obtain the magnitude and temporal shape of the hemodynamic responses. Comparing the fitted responses, we found that the deactivation responses to very short (1 or 2sec) stimuli OFF are very small in V1, much smaller than the corresponding positive signals produced by reversing the conditions (data not shown). Moreover, using the responses of short duration deactivations to predict the response to longer periods OFF by linear summation underestimates the responses of longer duration deactivation considerably. Thus the HRF for deactivation is much more non-linear than for positive BOLD effects.

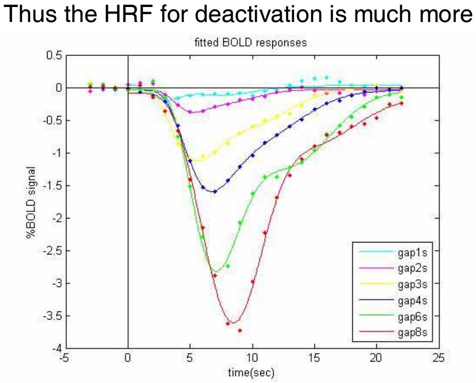

Figure1. Fitted BOLD responses in V1 for different durations of stimulus-OFF.

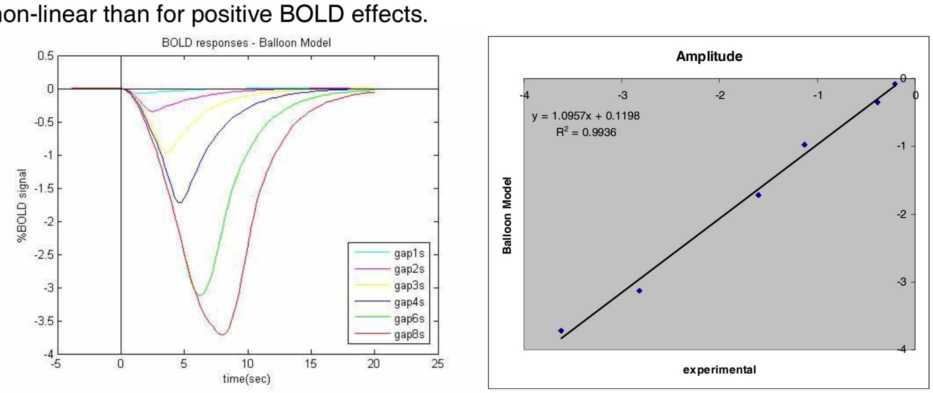

Figure2. Negative BOLD responses can be well modeled by modified Balloon model. Plausible consistence in amplitude between modeled and experimental BOLD responses was showed.

Discussion:

To account for our findings, we adapted the standard Balloon Model [Buxton 1998] in which flow is regulated in a manner that leads to over and under swings in blood oxygenation relative to the levels required to maintain metabolic demand. The key physiological variables incorporated in the model are the total deoxyhemoglobin (q) and the blood volume (v), both normalized to their values at rest. In this model, the fractional BOLD signal change is written as: $\Delta S/S=V_0[k_1(1-q)+k_2(1-q/v)+k_3(1-v)]$. The outflow from the balloon is treated as a function both of the balloon volume and the rate of change of the volume: $f_{out}(v)=v^{1/\alpha}+\tau(dv/dt)$, where τ controls how long this transient adjustment requires.

We assumed that the increase of Flow-in during inflation occurs more rapidly than the decrease of Flow-in during deflation, and selected the times $\tau_{\pm}$ of transient adjustment of the volume change as the time of Flow-in to increase or decrease. By assuming different time courses for flow decreases compared to flow increases, realistic non-linear responses that match the experimental data well can be obtained from the model (Figure2). It is clear that the effects of a transient deactivation are qualitatively and quantitatively different from the effects of a brief activation, and these findings have implications for the sensitivity for detecting signal decreases as well as for methods of data analysis.

References: **[1]** Liao CH, et al. NeuroImage 2002; 16:593-606. **[2]** Buxton RB, et al. MRM 1998; 39:855-864.