Quantitative Combined ASL/BOLD Imaging: Implications for the Interpretation of the BOLD Post-stimulus Undershoot

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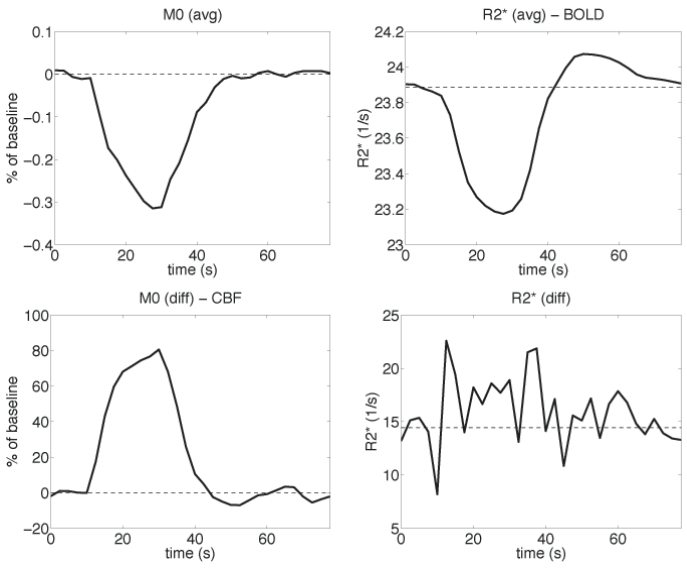
Purpose

A dual-echo spiral arterial spin labeling (ASL) technique provides simultaneous measurements of cerebral blood flow (CBF) and BOLD responses to brain activation, and has been applied in a calibrated-BOLD methodology to assess the coupling of CBF and the cerebral metabolic rate of O_2 ($CMRO_2$) [1-3]. However, the potential of this approach to provide a quantitative probe of the CBF and BOLD responses has not been fully exploited, in that cerebral blood volume (CBV) changes also affect the measured signals in a way that is potentially separable from the CBF and BOLD responses [4]. We tested whether a quantitative analysis, estimating R_2* and proton density separately for the tagged component and the total signal during visual stimulation, can shed light on the physiological origins of the BOLD post-stimulus undershoot.

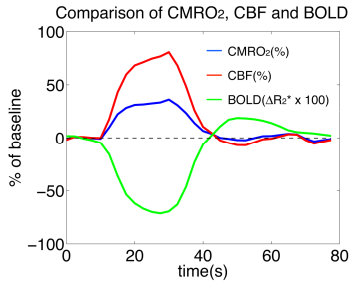
Methods

Image data from 8 healthy, adult subjects was obtained from a previous study at 3T of CBF/$CMRO_2$ coupling during visual stimulation based on simultaneous dual-echo acquisition of CBF and BOLD signals [3]. Each functional run consisted of a 60s rest period followed by four 20s task/60s rest cycles and a final 30s rest period. For each subject, an activation region of interest (ROI) was constructed with a GLM approach based on correlation of the model response with the CBF response data, including nuisance regressors for baseline drift and physiological terms based on cardiac and respiratory monitoring. Two ROI-averaged time series were constructed for each echo consisting of the temporal surround subtraction (labeled 'difference') and surround average (labeled 'average') of the tag and control images [5]. In previous analyses we have taken the first echo difference signal as the CBF signal and the second echo average as the BOLD signal [1-2]. In the current analysis we modeled the dual-echo difference and average time series separately as a single exponential decay with effective relaxation rates R_2* and effective proton densities M_0. R_2*(avg) and M_0(avg) are effective parameters for the overall voxel signal (tissue plus blood) and R_2*(diff) and M_0(diff) are effective parameters for just the tagged spins delivered by arterial flow, so M_0(diff) corresponds to the CBF response and R_2*(avg) corresponds to the overall BOLD response.



Results

The four curves of M_0(avg), R_2*(avg), M_0(diff) and R_2*(diff) are shown in the upper Figure. R_2*(diff), the relaxation rate of the tagged component, was lower than that of tissue, consistent with the expected lower R_2* of arterial blood compared to tissue. The primary activation response was a decrease in R_2*(avg) and an increase of M_0(diff) during the stimulus, corresponding to standard BOLD and CBF responses. In addition, there was also a slight decrease of M_0(avg), consistent with an effect similar to VASO [6] in which increased CBV is exchanged for tissue signal that is more relaxed due to a shorter T_1. There also was a trend for increased R_2*(diff) during activation, consistent with the tagged arterial spins moving farther down the vascular tree when flow is increased and being exposed to more deoxyhemoglobin (or perhaps more capillary tissue exchange). The post-stimulus undershoot period is dominated by an increase of R_2*(avg), a slight decrease of M_0(diff) consistent with a slight decrease of CBF, but no appreciable difference from baseline of M_0(avg). The M_0(diff) and R_2*(avg) curves were also analyzed with the Davis model [7], using the mean *M* value measured for the group [3] to estimate the dynamic time course of $CMRO_2$ (lower Figure).



Conclusions

In this study the BOLD post-stimulus undershoot was not associated with a slow recovery of CBV nor with a slow recovery of $CMRO_2$. Instead, it was consistent with a vascular origin due to a slight undershoot of CBF.

[1] Leontiev, Neuroimage 35:175, 2007; [2] Ances, Neuroimage 39:1510, 2008; [3] Perthen, Neuroimage 40:237,1998; [4] Woolrich MRM 56:891, 2006; [5] Liu, Neuroimage 24:207, 2005; [6] Lu, MRM 50:263, 2003; [7] Davis, PNAS 95:1834,1998