Dynamics of the Blood Oxygenation Response: Tissue CMR_{O2} Contributions and Impact for Functional MRI

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Introduction

The contribution of the principal physiological processes involved in the generation of the BOLD fMRI response, namely CBF, CBV and CMR_{O2}, have been studied independently using ASL and VASO methods as well as with contrast and physiological agents [1,2,3,4,5]. The objective of this work was to investigate the relative contributions of these processes in the generation of the BOLD fMRI response, in particular features like the post-stimulus undershoot and the initial dip, using a dynamic model that considers CBF, CBV and CMR_{O2} as dynamic independent variables [3,6,7]. CBF and BOLD fMRI data were supplied to the model and the viability of CMR_{O2}-sensitive functional MRI studies was also examined.

Methods

Nine subjects were scanned in a General Electric 3T MRI scanner. The subjects were asked to perform a visually cued motor task (60 s and 12 s of finger tapping followed by 60 s and 38 s of rest, respectively) while images were acquired using a two-echo gradient-echo FAIR acquisition [1]. The model was used to estimate the dynamic changes in CMR_{O2} from CBF and BOLD fMRI data and a hypercapnia manipulation [3]. A description of the model can be found in the literature [3,6,7]. Since CBV was not measured, two CBV responses were considered: (A) no CBV change, and (B) change in CBV according to Grubb's formula with a time constant of 12 s relative to the CBF response [8,9,10]. To examine the CMR_{O2} contribution to the BOLD fMRI data, the model was modified such that the CBF and CBV responses did not change from baseline in combination with the results obtained from (A) and (B) above; these tests were labeled (C) and (D), respectively.

Results

The steady-state change in CMR_{O2} was calculated to be 42.0% assuming that the CBV response did not change (case A). Alternatively, the steady-state change in CMR_{O2} was calculated to be 24.5% assuming that CBV changed according to Grubb's formula (case B). The average tissue CMR_{O2} dynamics were estimated for cases (A) and (B) as shown in Figure 1. The time constant for the average tissue CMR_{O2} response was determined to be 6.6 s and 7.7 s for cases (A) and (B), respectively. Modifying the model such that the CBF and CBV responses did not change from baseline (cases C and D), the CMR_{O2} contributions to the BOLD signal change were calculated and observed to be significant and temporally slow, reaching 50% of its steady-state amplitude after 10.0 s, on average, for both stimulus durations tested (see Figure 2).

Discussion

The results obtained suggest that the average tissue CMR_{O2} response is slow to evolve, similar to the CBF and CBV responses. The model attributed the BOLD post-undershoot feature to the slow CBV and CMR_{O2} responses (see Figure 2). The model predicted the BOLD initial dip under several conditions, including a temporal mismatch between the CBF and CMR_{O2} responses. In addition, a fast CBV response (2 s time constant) was tested and not favored by the model since it yielded a higher residual error. The results obtained demonstrate the estimation of the CMR_{O2}-related BOLD signal dynamics under different assumptions for the CBV response. The temporal changes observed suggest that BOLD fMRI studies with stimulus durations of a few seconds, perhaps even event designs (where the BOLD response still takes several seconds to peak), have a CMR_{O2} contribution that may be extracted from BOLD data.

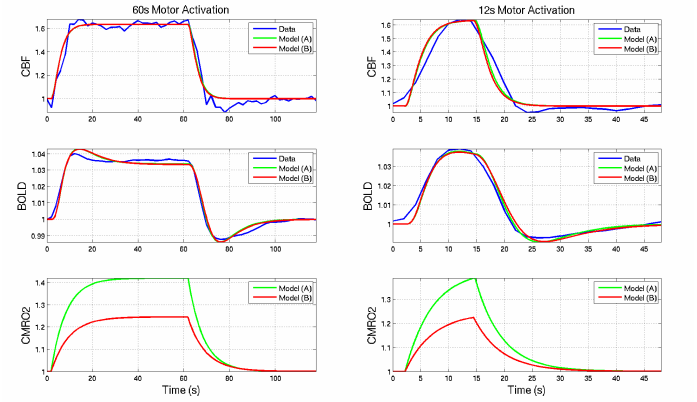

Figure 1: CMR_{O2} response estimates obtained from fits of the CBF (FAIR) and BOLD data for both 60 s (left panels) and 12 s (right panels) stimulus durations. CMR_{O2} estimates assuming no changes in CBV are shown in green (case A) and estimates assuming CBV changes according to Grubb's formula are shown in red (case B). Both cases estimated slow changes in CMR_{O2}. Fast changes in CMR_{O2} yielded high residual errors and were not favored by the model.

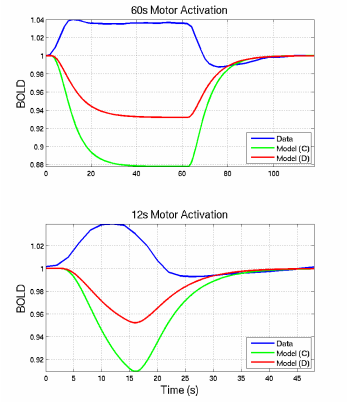

Figure 2: Comparison between the measured BOLD data and the calculated BOLD responses only due to the CMR_{O2} response assuming the CBV response did not change (case C, green line) and assuming CBV changed according to Grubb's formula (case D, red line). On average, the estimated CMR_{O2} contribution to tbe BOLD response was about 25% of its steady-state amplitude after 5 s.

References: [1] Kim SG, et al., MRM 34:293 (1995); [2] Lu H, et al., MRM 50:263 (2003); [3] Davis TL, et al., PNAS 95:1834 (1998); [4] Zhao F, et al., Neuroimage 30:1149 (2006); [5] Fukuda M, et al., Neuroimage 30:70 (2006); [6] Buxton RB, et al., MRM 39:855 (1998); [7] Valabregue R, et al., JCBFM 23:536 (2003); [8] Kim SG, et al., MRM 41:1152 (1999); [9] Grubb RL, et al., Stroke 5:630 (1974); [10] Mandeville JB, et al., MRM 39:615 (1998).