Estimating Dynamic CMRO2 Changes From CBF and BOLD fMRI Data

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Introduction Cerebral hemodynamics plays a very important role in the delivery of oxygen to brain tissue. Very little is known about the temporal characteristics of the process of delivery and consumption of oxygen. In addition, it is not clear how closely coupled are the changes in CMR_{O2} to the changes in neuronal function. The objective of this work is to estimate the dynamic changes in CMR_{O2} that take place as a result of evoked neuronal activity from CBF and BOLD fMRI data. Models of the regional cerebral hemodynamics and the magnetic signal disturbance caused by venous deoxy-hemoglobin were used in order to estimate the CBF, BOLD and corresponding CMR_{O2} changes. The coupling between the neuronal response and CMR_{O2} was investigated and the model predicted a slower CMR_{O2} response with respect to the neuronal response.

Model of the Hemodynamic Response The model consists of four parts that represent the various aspects of the hemodynamic response to a stimulus. The neuronal response is described by a modification of the stimulus temporal pattern to include possible neuronal adaptation (amplitude N and decay constant τ_n) and refractory responses (prolonged response w_{ex}) [1,2]. The vascular response to the neuronal changes is modeled with a first-order linear system (amplitude A, time constant τ_a). The response in oxygen delivery and consumption that follows neuronal activity is represented by the transport of oxygen from capillaries to tissue [3]. The ratio of the volume of these compartments (V_c/V_t) indicates the pool of tissue oxygen that can be readily consumed by the neurons. A visco-elastic behavior for the venous vasculature is assumed (parameter τ_v) [4]. The BOLD response is assumed to arise by a proportional relationship between R2* and the amount of venous deoxy-hemoglobin [5].

Methods A two-echo gradient-echo FAIR acquisition scheme was used to obtain simultaneous CBF and BOLD fMRI data with temporal resolution of 2 s. The TEs of the spiral readouts were 8/28 ms and TI of 1900 ms (2x inversion slab width). An axial slice through the motor cortex (7 mm) was scanned in all volunteers (n=10). The data of the slice-selective and non-selective FAIR conditions were linearly interpolated such that CBF and BOLD images were generated at each sample point. Study participants were instructed to perform a visually cued finger tapping task while inhaling 100% O_2 gas via a non-rebreathable mask (15 L/min) with stimulation periods of 60 s followed by 60 s of rest repeated 10 times. Images of CBF and BOLD were also acquired while the subjects remained at rest and the inhalation mixture was changed from 100% O_2 to 95% O_2 and 5% CO_2. All scans were performed in a General Electric 3.0 Tesla MRI scanner (Milwaukee, WI).

Steady-State Parameters The averaged functional FAIR and BOLD time series suggest motor stimulation produced steady-state CBF and BOLD changes of 64.4% and 3.6%, respectively (Fig. 1). The hypercapnia challenge produced FAIR and BOLD signal changes that estimated a calibration factor M of 0.18 so that the steady-state change in CMR_{O2} due to stimulation was ~23.7% [5]. The steady-state changes in CBF and CMR_{O2} were used in Monte Carlo simulations to determine likely estimates of the baseline blood flow (F_{in0}=57 ml/min), tissue oxygen tension (P_t=24.7 mmHg), permeability-surface area product (PS=6071 ml/min), oxygen extraction (E_0=0.33) and consumption rate (CMR_{O20}=3.8 ml/min) assuming normal physiology.

Results and Discussion To estimate the dynamic CMR_{O2} changes the following parameters were estimated: N, w_{ex}, A, τ_a, τ_v, V_c, V_t. The CMR_{O2} response was represented by a time constant ($\tau_r$and two scenarios were considered: (1) the CMR_{O2} response is as fast as the neuronal response (τ_r=0), (2) the CMR_{O2} response is slower than the neuronal response (τ_r>0). The results of the dynamic estimation process showed a slower CMR_{O2} response reduced the NMSE (normalized mean squared error) of the CBF and BOLD predictions versus a fast CMR_{O2} response by 19% (Fig. 1). A fast CMR_{O2} response produced larger NMSE estimates that included non-physiologic capillary-to-tissue volume ratios (< 0.1% vs. 0.6%). The model did not predict significant adaptation or refractory periods for the neuronal response (N<1%, w_{ex}<0.1 s). These estimates suggest the CMR_{O2} response is not as fast as the neuronal response, but moderately faster than the blood flow response (Fig. 1 right panels). This estimation of CMR_{O2} is limited by the models used and our current knowledge of the cerebral hemodynamics but these models can be used to increase our understanding of the hemodynamic mechanisms and exploit the information that can be extracted from the BOLD response under different physiological conditions.

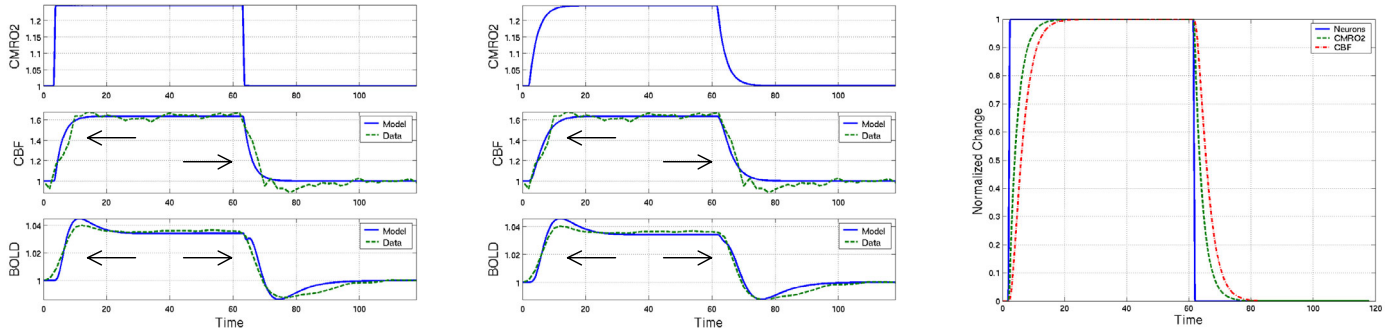

Figure 1: (Left, Middle) Model estimates of the CMR_{O2}, CBF and BOLD responses to 60 s of motor stimulation. A slower CMR_{O2} response (middle panels) improved the NMSE in comparison to an assumed fast CMR_{O2} response by 19% (left panels), evident over the transition regions. (Right) Normalized neuronal, CMR_{O2} and CBF responses presented in the middle panels indicating a moderately fast CMR_{O2} response with respect to the blood flow response.

References: [1] Logothetis N, et al., Nature 412:150 (2001); [2] Muller JR, et al., Science 285:1405 (1999); [3] Valabregue R, et al., JCBFM 23:536 (2003); [4] Buxton RB, et al., MRM 39:855 (1998); [5] Davis TL, et al., PNAS 95:1834 (1998).

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