Detection of CMRO2 Changes with and without Hypothesized CBF-CBV Relationship: an Event-Related fMRI study

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Introduction

For reaching the neuronal activity and better understanding the blood oxygenation level dependent (BOLD) response in functional magnetic resonance imaging (fMRI), the dynamic change of cerebral metabolic rate of oxygen ($CMRO_2$) has been explored recently. According to Hoge's model, a nonlinear coupling relationship between cerebral blood flow (CBF) and cerebral blood volume (CBV) is utilized to facilitate $CMRO_2$ estimation, as shown in Eq. [1] (1). However, the coupling relationship is derived from a previous report of animal experiment using positron emission tomography (PET), which may not be applicable in the event-related human studies (2). To examine this issue, the arterial spin labeling (ASL) and vascular space occupancy with tissue suppression (VAST)-based fMRI techniques were conducted in the event-related visual experiment for measuring the dynamic CBF and CBV independently (3, 4). Transient-state $CMRO_2$ change was estimated by our previous established model (5). To the end, no discrepancy was found among the temporal characteristics of $CMRO_2$ curves between with and without the assumed CBF-CBV relationship.

Methods

To estimate the dynamic $CMRO_2$, the adopted physiological model was expressed as Eq. [2]:

$$\frac{CBV}{CBV^0} = \left(\frac{CBF}{CBF^0}\right)^{\alpha} \quad [1]$$

$$\frac{\Delta BOLD}{BOLD^0} = M_v \cdot V_v \cdot (1-k) \cdot \left[1-\left(\frac{CMRO_2}{CMRO_2^0}\right)\cdot\left(\frac{CBF}{CBF^0}\right)^{-1}\cdot\left(\frac{CBV}{CBV^0}\right)\right]_{venule} + M_c \cdot V_c \cdot k \cdot \left[1-\left(\frac{CMRO_2}{CMRO_2^0}\right)^{2}\cdot\left(\frac{CBF}{CBF^0}\right)^{-2}\cdot\left(\frac{CBV}{CBV^0}\right)\right]_{capillary} \quad [2]$$

where '0' in the power term indicates the steady state, V_v and V_c are the blood volume fractions at the resting state for venules and capillaries, k is the active vessel fraction for capillaries, in the range $0 \le k \le 1$. The first term indicates the contribution from venules while the second term is referred to capillaries. M_v and M_c are field-strength-related constant for venules and capillaries, followed by Ogawa's Monte Carlo simulation of intravoxel dephasing (6): $M_v = 4.3 \cdot \omega_0 \cdot \Delta\chi \cdot (1-Y_v) \cdot TE$, and $M_c = 0.04 \cdot [\omega_0 \cdot \Delta\chi \cdot (1-Y_c)]^2 \cdot TE$, ω_0 is the resonance frequency in Hz, $\Delta\chi$ (=0.27 ppm) is the susceptibility difference between deoxygenated and fully oxygenated blood (7), ($1-Y$) denotes the deoxygenation fraction of the blood at the resting state, and TE is the echo time. Resting CBV of all blood vessels is assumed to be 5% and the arterial volume fraction (~37% of all vessels) is excluded in this model (8). k was calibrated by Kim's hypercapnia dataset (9). Eq. [1] is the common CBF-CBV relationship used in CMRO2 detection where α is equal to 0.38 derived from Grubb et al. (2). Functional experiments were performed on 1.5T Magnetom Vision (Siemens, Erlangen, Germany). Even-related visual stimulation with 8-Hz frequency checkerboard was delivered to 3 subjects through an LCD goggle (1s stimulation, intertrial interval=20s, 22 trials for each measurement). Single slice with 8 mm slice thickness was sectioned along the calcarine fissue, FOV=192×192 mm^2, MTX=64×64. BOLD was acquired by gradient-echo echoplanar image (GE-EPI), TR/TE=1000/60 ms, CBF was derived by flow-alternating inversion recovery (FAIR)-EPI with TI (inversion time)/TR/TE=1200/4000/29 ms, and CBV was estimated by non-selective inversion recovery EPI with TI/TR/TE=508/2000/9.3 ms, assuming 5% resting CBV and 5% cerebrospinal fluid (CSF) volume fraction. Temporal shift of the paradigm were performed in the CBF and CBV sequences to reach the temporal resolution of 1s. Statistical significant activations ($p \le 0.05$, cluster number = 3) were selected to process the curve averaging.

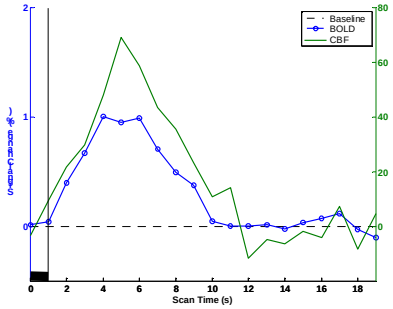

Fig. 1: Averaged temporal responses (n=3) of BOLD (blue) and FAIR (green) to 1s visual stimulation (black bar and vertical line).

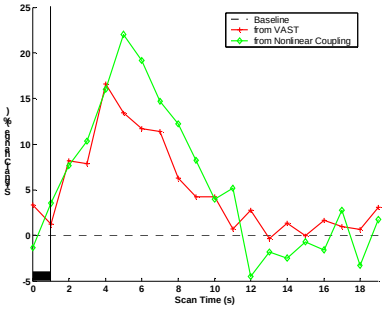

Fig. 2: Time courses of dynamic CBV change estimated by VAST exp (red) and by the CBF-CBV assumption (green).

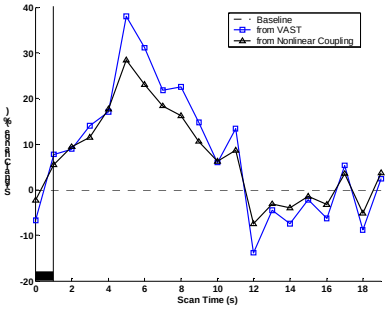

Fig. 3: Estimated CMRO2 curves by Eq. [2] with (black) and without (blue) the hypothesized CBF-CBV relationship.

Results

Fig.1 shows the averaged time courses of BOLD and CBF change over subjects and trials. BOLD response reached the peak at 5 s and return to baseline at 10s after the stimuli emergence. Two CBV time courses were calculated and sketched in Fig. 2, where red curve is the estimated CBV by the VAST experiments and the green curve is the CBV variation following the CBF information by Eq. [1]. Distinct onset and falling times are observed between the two CBV curves, which indicate the estimation error of adopting the CBF-CBV relationship at transient state. Concerning the signal intensity, the CBF-CBV relationship probably caused a 10% difference on the dynamic CBV changes. In Fig. 3, black curve is the result of $CMRO_2$ estimated by the assumption of Eq. [1] whereas the blue curve is the estimated $CMRO_2$ without CBV assumption. Although the dynamic CBV changes from the two models are differentiable, there is no explicit differentiation between the temporal characteristics of estimated $CMRO_2$ curves. Only the enlarged signal change in the blue curve is observed due to the lower corresponding CBV signal changes.

Conclusion & Discussion

In this study, we explored two models for estimating dynamic $CMRO_2$ change at transient state. One adopted the hypothesized CBF-CBV relationship and the other utilized a newly developed CBV-sensitive sequence. As the result, no explicit differentiation was discovered among the temporal characteristics of $CMRO_2$ curves. Several considerations are discussed below. First, the temporal delays of VAST and FAIR caused by TI were not included in this preliminary work, which also affected the temporal estimation error. Second, the CBV information of VASO-based fMRI contains the dynamic change of arterial blood volume, which should not be considered according to basic assumption of Eq. [2]. Further investigations shall be conducted to improve the accuracy of the transient-state $CMRO_2$ estimation.

References

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