Steady-state to transient change of CMR_{O2}: Dynamic calibrated fMRI at 11.7T

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INTRODUCTION

Correlation and/or deconvolution methods have been used to examine the dynamic coupling between neuronal activity and fMRI signals. These approaches have resulted in heuristically-based mathematical models for describing BOLD and its underlying physiology [1-3]. We are investigating the relationships between the complex components of the BOLD signal (e.g., CBF, CBV, CMR_{O2}) and neuronal activity (e.g., MUA, LFP), both at steady-state and transiently. The aim of this study was to examine the degrees of correlation from the single event to the block design paradigm. By control of the stimulus frequency and the number of stimulus impulses, we hypothesized that it should be possible to extrapolate if there are CMR_{O2} changes that underlie BOLD for extremely short events. This required sensitive measurements of BOLD, CBF, CBV, and LFP from the anesthetized rat.

METHODS

Animal preparation*:* Sprague-Dawley rats were tracheotomized and artificially ventilated (70% N_2O, 30% O_2). During the preparation halothane (1-2%) was used for induction. Intraperitoneal lines were inserted for administration of α- chloralose (46±4 mg/kg/hr) and *D*-tubocurarine chloride (1 mg/kg/hr). An arterial line was used for monitoring systemic physiology (pH, pO_2, pCO_2) throughout the experiment. ***Forepaw stimulation:*** The stimulation ranged from a single pulse to several pulses up to a block design. Each pulse was 2 mA in amplitude and 0.3 ms in duration. The frequency ranged from 1.5 to 6 Hz. ***fMRI, CBF, CBV*** *(n=8):* All fMRI data were obtained on a modified 11.74T Bruker horizontal-bore spectrometer (Billerica, MA) using a ^{1}H resonator/surface coil RF probe. All images were acquired with gradient echo EPI (TR/TE=1000/15 ms). Details of BOLD, CBF, and CBV measurements are in ref. [4]. ***Neurophysiology*** *(n=12):* The rat was placed in a stereotaxic holder on a vibration-free table inside a Faraday cage. Tiny burr holes above the contralateral and ipsilateral somatosensory regions [4.4 mm lateral and 1.0 mm anterior to bregma] were thinned and tungsten microelectrodes (FHC, Bowdoinham, ME) were inserted at a depth of layer 4 with stereotaxic manipulators (Kopf Instruments, Tujunga, CA). The signal was then digitized with a μ-1401 interface using SPIKE-2 software [4]. The data were filtered to obtain both LFP and MUA. A laser-Doppler probe (Oxford Optronix, Oxford, UK) was used for dynamics of red cell flux, concentration, and velocity.

RESULTS: We found variable dependencies of each component (BOLD, CBF, CBV, LFP) with the inter-pulse interval (IPI), as shown in Fig.1. The CBV-IPI relationship was most linear, whereas the CBF-IPI relationship was most non-linear, similar to the LFP-IPI relationship. The BOLD-IPI relationship was between extremes for CBV and CBF. The LFP data showed interesting patterns. There was an evoked LFP signal for each individual stimulus pulse (data not shown). However alternate evoked LFP signals (i.e., ■ vs. ▲ in the expanded LFP signal shown in the inset of Fig.1) were attenuated for stimuli with multiple pulses at higher frequencies, which suggest that for extremely short stimuli the evoked LFP response may not show the same linearity as observed for longer stimuli [1-3]. We calculated CMR_{O2} on the assumption that there was a missing component to account for the non-linearity in CBF and BOLD vs. CBV. Surprisingly we found that CMR_{O2} contributed to BOLD even with IPI of less than 200 ms (i.e., 6 Hz).Furthermore, coupling between CBF-CMR_{O2} at short IPI was better than at long IPI. The agreement between CMR_{O2}-LFP provided a pseudo validation for the CMR_{O2} changes that underlie BOLD for such short stimuli. These results suggest that BOLD at high field of 11.7T has the sensitivity to reveal a CMR_{O2} component for extremely short events.

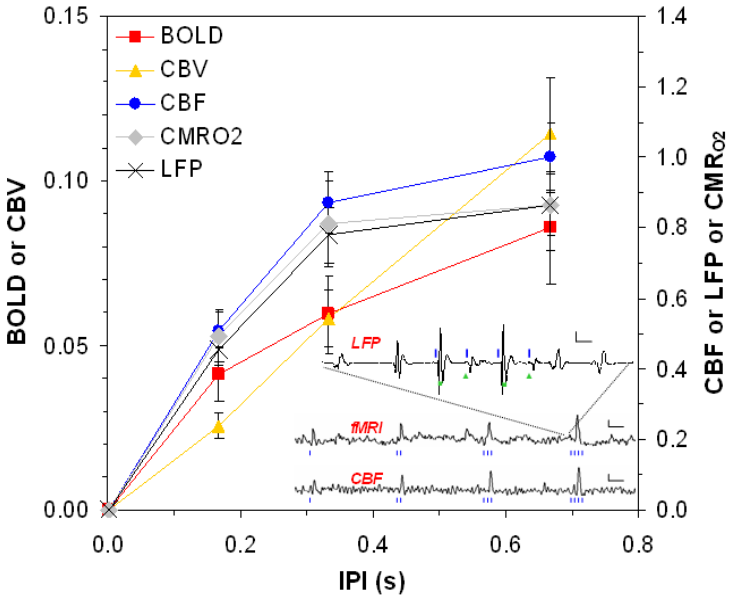

Fig 1: BOLD, CBV, CBF, and LFP as a function of IPI to calculate changes in CMR_{O2}. *Inset:* Responses measured from layer 4 during stimulation with 1, 2, 3, and 4 pulses fMRI and CBF dynamics are from single trial run. LFP signal is an expansion of the 4 pulse experiment.Vertical/horizontal bars for fMRI, CBF, LFP: 2%/20s, 20%/20s, 200 mV/200ms.

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