BOLD impulse response functions in the somatosensory cortex: Implications for CMR_{O2} calculation

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INTRODUCTION

Quantitative mapping of changes in CMR_{O2} with BOLD calibration has become a popular modality for studying functional brain activity [1] because it is proportional to changes in energy consumption associated with alterations in neuronal activity induced by different type of stimulations [2]. The calibrated fMRI is based on a tissue oxygen extraction model [3-4]. This model includes measured or modeled hemodynamic parameters (CBV, CBF). The intensities and shapes of the responses are different in different areas of the cortex, but it is unclear whether these responses will differ only because of the different neural responses. If the latter is true, than the same CMR_{O2} calibration can be used through different cortical areas. We measured BOLD and LFP signals in the forelimb and the whisker barrel cortex in separate groups of α-chloralose anesthetized rats and calculated the impulse response functions (or transfer functions) with convolution analysis between these modalities. We use the assumption that the transfer function can linearly convert the electrical activity to the co-localized BOLD response, therefore similar transfer functions can establish the same CMR_{O2} calibration.

MATERIALS and METHODS

Sprague-Dawley rats were tracheotomized and artificially ventilated (70% N_2O, 30% O_2). The anesthesia was switched to i.p. α-chloralose (80mg initial dose, then 40 mg/kg/hr) from Halothane or Isoflurane (1-2%) after the surgery. A femoral arterial line was used for monitoring blood pressure, acid-base balance and blood gases throughout the experiment. ***Stimulation:*** Copper needles were inserted below the skin of the forepaw. Each stimulus train used 2 mA in amplitude, with 3 Hz frequency, and 0.3 ms in duration. For whisker stimulation we used air-puffs through a solenoid controlled plastic tube [5]. 8Hz of stimulus frequency was selected. All stimulus presentation lasted 30s and was controlled by a μ-1401 analog-to-digital converter unit (CED, Cambridge, UK) running custom-written script. ***BOLD*** *(n=13):* 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=1000/12.53 ms). All fMRI data were subjected to a translational movement criterion [6]. ***Electrophysiology*** *(n=33):* In a separate group of animals after surgery the rat was placed in a stereotaxic holder (Kopf Instruments, Tujunga, CA) on a vibration-free table inside a Faraday cage. Tiny burr holes above the somatosensory forelimb region [4.4 mm lateral and 1.0 mm anterior to bregma] and above the whisker barrel region [5 mm lateral and 2.5 mm posterior to bregma] were drilled and high impedance microelectrodes (2-4 MΩ) were inserted with stereotaxic manipulator. Electrical signals were digitized with CED μ-1401 using Spike 2 software (Cambridge Electronic Design, Cambridge, UK) at 20 kHz. Local field potentials (LFP) were obtained applying low pass filter (<150Hz) to the raw time series then integrated into 0.02s bins. ***Convolution analysis***: The transfer function, $h(t)$, can be achieved by deconvolution between the LFP and the BOLD signal. A modified form [7] of the gamma variate function (GVF) was used for transfer function model [8]. The parameters of the transfer function were calculated with iterative steps within Matlab (Natick, MA). The input function was defined as the average of the LFP series, where the individual events were normalized to the largest local field potential.

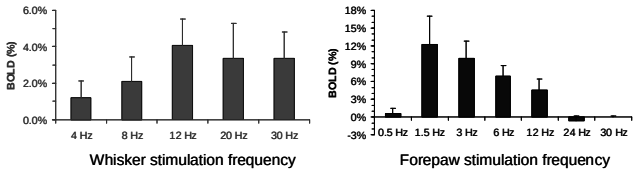

Fig. 1 BOLD frequency response curves [5]

RESULTS and DISCUSSION

The frequency tuning curves for forepaw and whisker stimulations are different [5] (Fig 1). We selected those stimulation frequencies which are near the maximum of their peak responses. We studied the responses only in the middle (III-IV) cortical layer, from where the electrical activity was measured (Fig 2A and 2B). The activation distribution between the lower, middle, and upper cortical layers was not equal, 1:1.78:1.08 respectively for the whisker barrel and 1:4:4.58 respectively for the forepaw area. The BOLD response and LFP activity for whisker stimulation were weaker than that for the forepaw stimulation. However their normalized values were correlated very well (Fig 2 right column, r^2 is 0.86 and 0.99, respectively). Transfer functions were calculated for both areas (Fig 2C). The precision of the simulated signal was checked by the comparison of the residual signal (i.e. difference between the modeled and measured signal) and the standard deviation (SD) of the measured signal. We considered the precision of the model adequate when the root mean square of the residual signal was smaller then the mean SD of the measured signal (Forepaw: 0.58 vs. 0.2, Whisker: 0.41 vs. 1.36). Despite the similar characteristics of the transfer functions and the high correlation of the normalized signals, the marked hysteresis in the impulse response function indicates caution in the CMR_{O2} calibration.

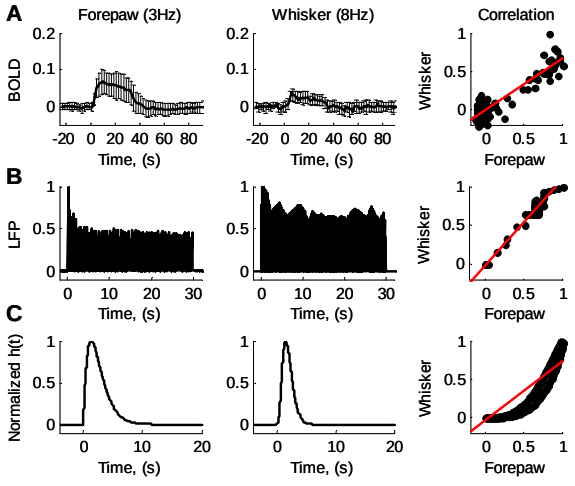

Fig 2. Comparison of the forepaw and whisker stimulations

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