Neurometabolic and neurovascular couplings across cortical layers of rat brain

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INTRODUCTION

Understanding of neurovascular and neurometabolic couplings is essential for the accurate interpretation of functional imaging [1]. The studies to describe neurovascular and neurometabolic couplings are focused a given region in the cortex [2,3,4]. High-field fMRI provides increased spatial specificity of evoked hemodynamic responses [5] opening the way to study the trans-cortical description of neurovascular and neurometabolic couplings. Here we measured hemodynamic responses (CBF, CBV, BOLD) and extracellular neural responses, such as local field potentials (LFP) or the multi-unit activities (MUA) to forepaw stimulation in three different layers of the rat somatosensory cortex. Additionally we calculated cerebral metabolic rate of O_2 consumption (CMR_{O2}) with calibrated fMRI at 11.7T [6]. These layer specific multi-modal measurements allowed identifying trans-cortical neurovascular and neurometabolic couplings.

METHODS

Animal preparations: Anesthetized Sprague-Dawley rats were tracheotomized and artificially ventilated (70% N_2O, 30% O_2) with 55-80 beat/minute rates. The anesthesia was switched to i.p. α-chloralose (80mg initial dose, then 40 mg/kg/hr) from 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. Electrical forepaw stimulations were applied (0.3ms, 3Hz, 2mA) for 30s duration. ***Neurophysiological measurements:*** Rats were placed in a stereotaxic holder on a vibration-free table inside a Faraday cage. Tiny burr holes above the contralateral somatosensory regions [4.4 mm lateral and 1.0 mm anterior to bregma] were drilled and high impedance tungsten microelectrodes (FHC Inc, Bowdoinham, ME) together with micro laser-Doppler probes (Oxford Optronics, Oxford, UK) were inserted gradually into the cortex (upper layer: 0.3 mm, middle layer: 1 mm, lower layer: 1.5 mm) Neural signals were recorded with a μ1401 A/D converter unit using Spike2 software (CED, Cambridge, UK). MUA and LFP were extracted from the raw signal with band-pass (300-3000Hz), and low pass (<150 Hz) electronic filter, respectively (Krohn-Hite, Inc). CBF data were calculated from LDF signals. ***fMRI measurements:*** All fMRI data (BOLD and CBV) were obtained on a modified 11.7T Varian horizontal-bore spectrometer using a 1H surface coil (Ø = 1.4 cm). The images were acquired with gradient echo EPI sequence (TR/TE = 1000/15) [4]. ***CMR_{O2} calculations:*** CMR_{O2} signals were derived from the BOLD, CBV and CBF signals using the calibrated fMRI equation (M=0.4) [6]. ***Transfer functions:*** Transfer functions of BOLD, CBV, CBF signals were calculated using MUA and LFP separately as input functions in an iterative process [4]. These transfer functions were modeled as gamma variate functions [7].

RESULTS

Our layer specific hemodynamic signals show good agreement with those in the literature [5], but both BOLD and CBV, which varied considerably across layers, were uncoupled with layer specific neural activities (Figure 1). There is a remarkable difference between the MUA and LFP responses across the layers. MUA is weakest in the superficial layers, while LFP is equally strong in all layers. CBF responses are strongly correlated with LFP, whereas the CMR_{O2} responses followed the MUA pattern throughout the cortical layers.

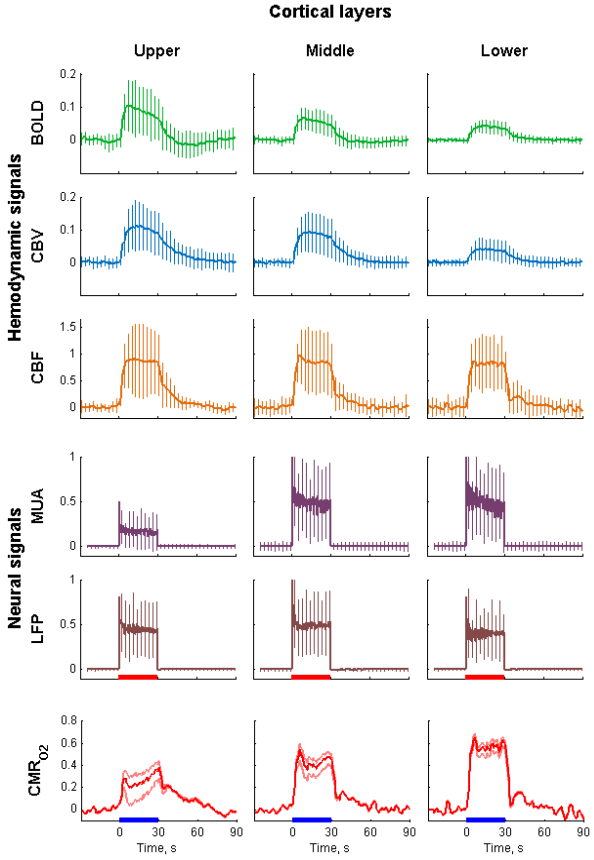

Figure 1. Mean and SD of the measured hemodynamic and neural functional responses are shown in three cortical layers of the somatosensory cortex Using calibrated fMRI equation [6] CMR_{O2} signals were calculated.

DISCUSSION

To confirm these experimental observations of CBF/LFP and CMR_{O2}/MUA having different spatial distributions, we performed a transfer function analysis [4] of multi-modal signals to identify neurovascular and neurometabolic couplings, since mere correlation of two different physiological modalities can be misleading [8]. Stability of layer-specific transfer functions between LFP and CBF signals indeed proved strong neurovascular coupling across layers are based on the LFP property of neural activity. Furthermore we used Wiener deconvolution analysis [9] to independently identify the predicted neural origins of the CMR_{O2} signal. The predicted neural signals through the cortex are ~2 times better correlated with the measured MUA than the LFP signals. Therefore while the trans-cortical neurovascular coupling is based the presynaptic neural activity which is considered to be the origin of the LFP signal, the trans-cortical neurometabolic coupling is related to the signaling property of neurons.

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