Multi-modal functional studies in rat somatosensory cortex: Heterogeneity across layers

P. Herman[1,2], B. G. Sanganahalli[1], F. Hyder[1,3]

[1]Diagnostic Radiology, Yale University, New Haven, CT, United States, [2]Institute of Human Physiology and Clinical Experimental Research, Semmelweis University, Budapest, Hungary, [3]Biomedical Engineering, Yale University, New Haven, CT, United States

INTRODUCTION

High resolution activation maps of columnar structures during sensory stimulation in rats obtained by 2-deoxy-glucose autoradiography [1] and fMRI [2], which reflect localized changes in metabolism and oxygenation, reveal heterogeneity across cortical layers. These results are interpreted as supporting the hypothesis of neurometabolic-neurovascular coupling [3]. To date layer-specific comparison of neuronal activity and neurometabolic-neurovascular responses are lacking possibly due to method limitations. We have measured neurometabolic-neurovascular responses (BOLD, CBF, pO_2) and electrical activity (AP, LFP) in rat during 30 s forepaw stimulation, as a function of cortical depth at 11.7T.

MATERIALS and METHODS

Animal preparation: Artificially ventilated Sprague-Dawley rats (male; n = 43) were anesthetized with α-chloralose (40 mg/kg/hr) and *D*-tubocurarine chloride (0.5 mg/kg/hr; i.p.). An arterial line was used for monitoring blood pressure and taking samples for blood pH, pO_2, pCO_2 throughout the experiment. The forepaw stimulation consisted of 3 Hz pulses with 2 mA amplitude where each pulse was 0.3 ms in duration. ***fMRI measurements:*** All fMRI experiments were conducted on a 11.7T spectrometer (Bruker, Billerica, MA) using a ^{1}H resonator/surface-coil radio-frequency probe [4]. Gradient-echo EPI data (TE=15ms) were acquired with TR of 1 s. The images were collected in matrix 64×64 spatial resolutions; the slice thickness was 2 mm, the number of slices was 3. The middle slice position was selected at the level of Bregma and only this slice was used in the analysis. Data were collected in 120 s windows: 30 s before and 60 s after the 30 s forepaw stimulation. ***Neurophysiology measurements*:** Electrical activities (AP and LFP) were measured by high impedance microelectrodes (2 MΩ; 1 μm tip) simultaneously with laser Doppler flowmetry and pO_2 responses with optical and oxygen fluorescence probe (Ru; 485/600 nm), respectively (Oxyflo and Oxylite, Oxford Optronix, UK). All signals were then digitized (>20 kHz) with a μ-1401 interface using SPIKE-2 software.

RESULTS and DISCUSSION

Laminar variations of the BOLD, CBF, AP, and pO_2 responses from a single rat are shown in Fig. 1 and the averaged responses are shown in Fig. 2. Laminar-specific averaged responses of AP (Fig. 2A), LFP (Fig. 2B), CBF (Fig. 2C), and pO_2 (Fig. 2D) during 30 s stimulation across all layers generally show some agreement, but there were some differences. For fMRI data, only voxels surpassing the statistical threshold of $P<0.05$ were used for the analysis. On the ipsilateral side the numbers of responding voxels were significantly smaller than on the contralateral side. All of the coronal slices showed BOLD responses, with decreasing intensities from top to bottom layers. The largest BOLD response was obtained within the coronal slice located near the Bregma. However in the anterior slice (supplementary somatosensory areas) there were significant BOLD responses on contralateral side for the top layers. The AP and LFP signals in the middle layers showed a slight depressed activity lasting ~5 s immediately following stimulation offset. The LFP signal in all layers showed a rapid rise and then decay to a plateau within ~5 s immediately following stimulation onset (Fig. 2B), which was different from the laminar responses of the AP signal (Fig. 2A). The CBF changes were uniform across most layers (Fig. 2C), whereas the pO_2 signal was significantly delayed compared to the other signals in top and bottom layers (Fig. 2D). Although the dynamics of the different mutli-modal signals were generally correlated, these results have significant implications for dynamic modeling of the BOLD signal [5].

Fig. 1

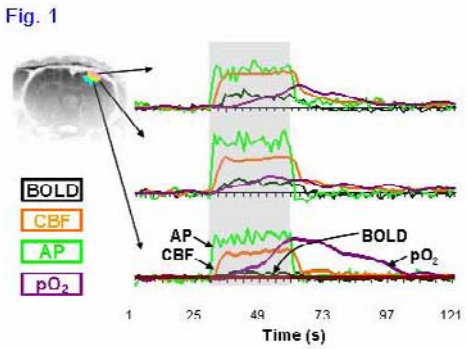
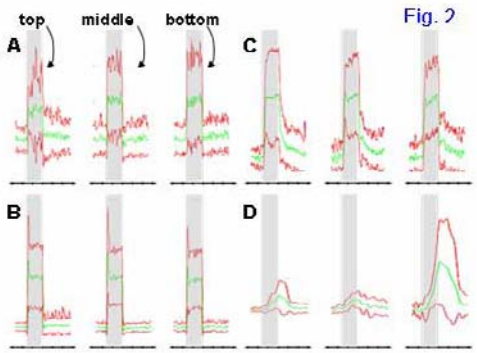


Fig. 2



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