Multi modal-functional studies in rat somatosensory cortex: Heterogeneity due to stimuli

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INTRODUCTION

High resolution activation maps of columns during sensory stimulation in rats obtained by 2-deoxy-glucose autoradiography [1] and fMRI [2], which reflect localized changes in CMR_{glc} and BOLD signal (i.e., CMR_{O2} and CBF indirectly), reveal heterogeneity across cortical layers. These results are interpreted as supporting the hypothesis of neurometabolic-neurovascular coupling [3]. To expand the heterogeneity examination of the neurometabolic-neurovascular coupling, data are needed to describe the effects of the various stimuli to the functional activation. We have measured neurometabolic-neurovascular responses (BOLD, CBF, pO_2) and electrophysiological responses (action potential: AP, local field potential: LFP) in rats during 30 s forepaw stimulation in the layer 4 of the somatosensory cortex, as a function of stimulation parameters.

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. ***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. ***Electrophysiology 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. ***Stimulation parameters:*** The parameters of the forepaw stimulation were as follows. The frequency of the stimulus ranged from 1, 3, and 9 Hz. The amplitudes of the stimuli were 0.2, 2, and 10 mA. The duration of each stimulus pulse was 0.3 ms.

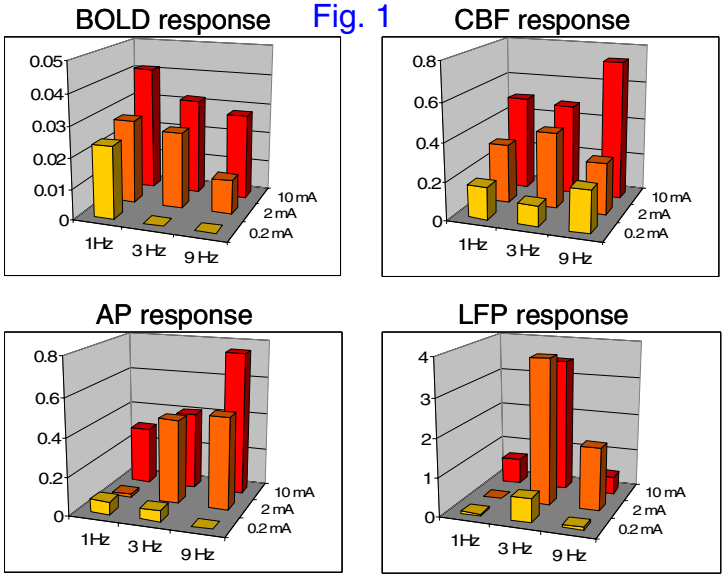

Fig. 1

RESULTS and DISCUSSION

The result of the BOLD, CBF, and electrical activity changes are shown in Fig. 1. The tissue pO_2 responses are not shown in however, we found marked responses only with the 3Hz/2mA and 10mA, and 9Hz/10mA stimulus parameters. For BOLD, only voxels surpassing the statistical threshold of $P<0.05$ were used for the analysis. Generally for the BOLD response, we found that increasing the stimulation amplitude elevated the response, whereas increasing the frequency decreased the response. However at 0.2 mA stimulation with 3 and 9 Hz no significant changes in the BOLD signal were detected. The neurophysiologic responses (CBF, AP, LFP) showed very weak frequency dependency for the 0.2 mA stimulation, indicating that the fMRI response threshold may have been reached with these stimulus parameters. However there is a general trend with all signals that the increased stimulation amplitude usually increased the elicited response at all frequencies. To compare the dynamic pattern of the responses, we compared the percent of the averaged normalized differences (PAND). The PAND parameter compares the correlation of different responding patterns, irrespective of the actual magnitude of a given response. The correspondence between the BOLD-CBF, BOLD-AP, and BOLD-LFP patterns were ~0.16, ~0.2 and ~1.0, respectively, for the PAND parameter. The CBF-AP and CBF-LFP patterns corresponded to ~0.08 and ~0.93, respectively, for the PAND parameter. Therefore we can conclude that in our experimental setup there were good correspondence between an AP, CBF, and BOLD signal responses.

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