Modality-specific frequency dependency of the rat somatosensory cortex assessed by fMRI

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INTRODUCTION

Somatosensory cortex integrates input from different parts of the body into somatotopic maps. The whisker-to-barrel cortex pathway in the rodent has a number of features that make it an attractive experimental model for understanding sensory perception [1,2]. If deflections are applied to the whisker pad in a precise fashion, the structure of receptive fields can be mapped in a highly quantitative manner [3,4]. Activation of the somatosensory cortex during electrical stimulation of the rodent forepaw [6,7], hindlimb [8], and whiskers [4,5] have been studied previously. To date, the frequency dependency of whisker and forepaw stimulation has not been demonstrated in the same animal due to the difference in the experimental setup during forepaw and/or whisker stimulations. We developed a naturalistic stimulation of the whiskers using home built non-magnetic whisker stimulation using air-puffs and measured the stimulation frequency-dependent BOLD responses from the whisker barrel cortex and the forepaw area in the same animal.

MATERIALS and METHODS: ***Animal preparation****:* Sprague-Dawley rats were tracheotomized and artificially ventilated (70% N_2O, 30% O_2). During the animal preparation halothane (1 to 2%) 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 physiology (blood pH, pO_2, pCO_2) throughout the experiment. ***Whiskers stimulation:*** Contralateral whiskers were trimmed to a length of ~14 mm. Air puffs were used to stimulate the whiskers. Airpuffs were generated from pulses of compressed air, which could be delivered in a computer-controlled way by inbuilt solenoid unit (Solenoid valves, Cole-Parmer Instrument). Air puffs were applied through stiff micropipette tip with a 2 mm opening positioned 15-20mm lateral from whiskers. Under these conditions, the air puff stimuli deflected all the whiskers by 2 mm (rostral-caudal) which were glued with a tiny adhesive tape. All stimulus presentation was controlled through a μ-1401 (CED, Cambridge, UK) running custom-written script. Whiskers stimuli were presented at 4, 8, 12, 20 and 30 Hz for duration of 30 s and were interleaved with an inter-stimulus interval (ISI) of 300s (i.e., time form end of one stimulus to the start of next). This very long ISI was used to ensure that there were no interaction effects between adjacent stimuli. ***Forepaw stimulation:*** Stimulation was achieved by insertion of thin needle copper electrodes under the skin of the forepaw. Electrical stimulation consists of 0.3ms square wave pulses provided with an isolator stimulator (World Precession Instruments, FL, and USA). Variation of functional response is achieved by varying the frequency (0.5 – 30 Hz) of the stimulus. The stimulus was controlled with a computer by custom written script with 30s off 30s on block design. ***fMRI (n=8):*** All fMRI data were obtained on a modified 11.7T Bruker horizontal-bore spectrometer (Billerica, MA) using a ^1H surface coil (Ø = 1.4 cm). The images were acquired with gradient echo EPI sequence (TR/TE = 1000/15).

RESULTS and DISUSSION

We investigated frequency dependent activations of the rat somatosensory cortex (at 11.7T) for two sensory modalities, whisker and forepaw, in the same subject. We found variable dependence of stimulus frequency on the BOLD response during naturalistic whisker stimulation using air puffs and electrical forepaw stimulation. We used 30 s block design stimulation protocols of whisker movement (rostral – caudal, 2 mm) and forepaw stimulation (2 mA, 0.3 ms) with varying frequencies of up to 30 Hz. During whisker stimulation, we observed linear increases in the BOLD response with increasing frequencies of up to 12 Hz beyond which saturation was observed. On the contrary, with forepaw stimulation the BOLD response was largest at 1.5 Hz and decreased with increasing frequencies. The data demonstrate differences in the frequency dependent BOLD response during forepaw and whisker stimuli and provide the framework to study mechanisms of coupling between neuronal activity and blood flow in these regions.

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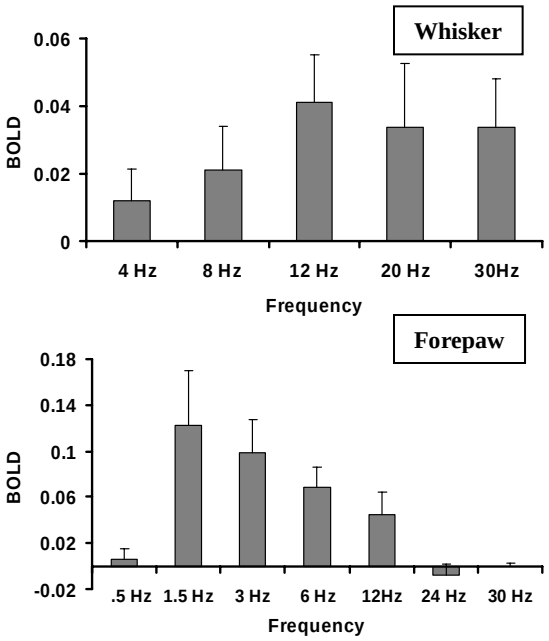

Fig. 1. BOLD responses during whiskers (rostral – caudal; 2mm) (n=6) and forepaw (2 mA, 0.3 ms) (n=6) stimulation with varying frequencies.