Sensory integration studies in rodent by fMRI: Intra- and inter-hemispheric effects

B. G. Sanganahalli[1], P. Herman[1,2], H. Blumenfeld[3], and F. Hyder[1,4]

[1]Diagnostic Radiology, Yale University, New Haven, CT, United States, [2]Institute of Human Physiology and Clinical Experimental Research, Semmelweis University, Budapest, Hungary, [3]Neurology, Yale University, New Haven, CT, United States, [4]Biomedical Engineering, Yale University, New Haven, CT, United States

INTRODUCTION

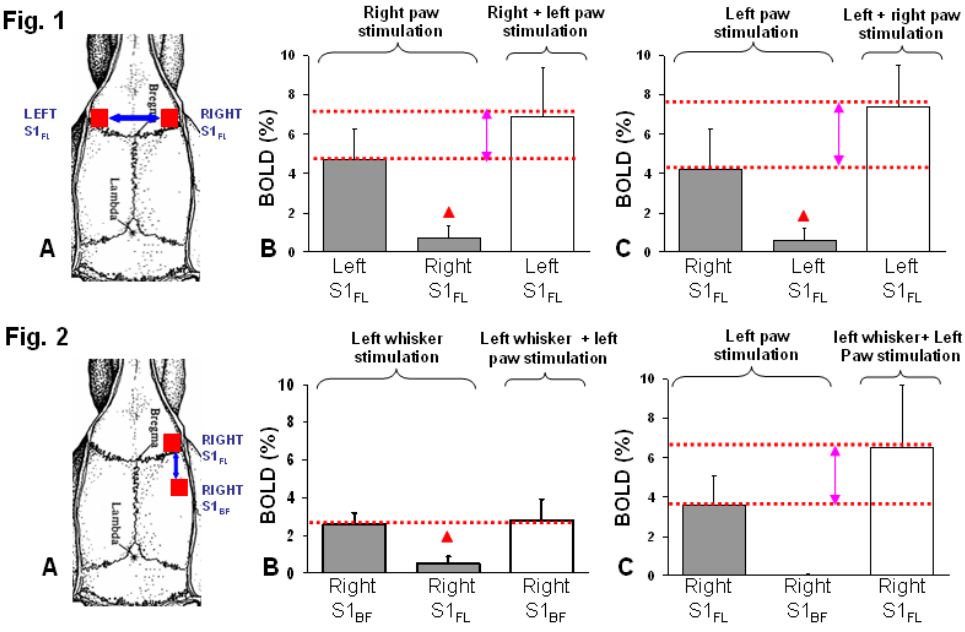
The somatosensory cortex of the rat is an appropriate model to investigate cortical integration because of well defined anatomical structure and function. Earlier and most recent studies have demonstrated the role of somatosensory cortex in integrating different sources of tactile input and have been primarily investigated by inferring the results from extracellular recordings [1-6]. Bilateral unit recordings in primary somatosensory cortex (S1) of anesthetized rodents have demonstrated substantial cross talk between cortical hemispheres suggesting that bilateral integration could occur at S1 [4]. It is well known that callosal cross projections integrate the two S1 hemispheres [7-8]. Studies by Ogawa et. al using bilateral measurements from the forepaw somatosensory cortex of rat have shown that prior activation of right forepaw greatly reduced neuronal and the BOLD evoked response to left forepaw stimuli [9]. A central hypothesis in sensory integration studies is that stimuli may have very different neurophysiologic outcome(s) when paired with an event in the same or another modality. Here we asked the question whether continuous activation of one forepaw has any consequence on the subsequent activation on the other forepaw or continuous activation of whiskers of the same side of the cortex has any effect on the forepaw area and vice versa. We designed an experiment to test for possible sensory interactions between left and right forepaw ($S1_{FL}$) regions as well as forepaw ($S1_{FL}$) and whisker ($S1_{BF}$) regions of the same side of the somatosensory cortex.

MATERIALS and METHODS

Animal preparation: Sprague-Dawley rats were tracheotomized and artificially ventilated (70% N_2O, 30% O_2). During the animal preparation isoflorane (2 to 3%) was 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. *Forepaw stimulation* (2mA, 0.3 ms, 3Hz): Stimulation was achieved by insertion of thin needle copper electrodes under the skin of the forepaw. *Whisker stimulation* (8Hz): Contralateral whiskers were trimmed to a length of ~14 mm. Air puffs were used to stimulate the whiskers. Air puffs were generated from pulses of compressed air, which could be delivered in a computer-controlled way by a solenoid unit (Solenoid valves, Cole-Parmer Instrument). The details of the forepaw and whisker stimulation procedure are available in our previous paper [10] *Sensory integration stimulation paradigm:* Stimulation of one region alone (left or right forepaw or left whisker) was performed for 90 s; followed by the stimulation of a second region for 30 s. Left paw or (left whisker) and right forepaw stimulations were staggered and the stimulus was controlled with a computer by custom written script. *fMRI (n=16):* 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 DISCUSSION

Independent stimulation of forepaw or whisker activated the contralateral $S1_{FL}$ or $S1_{BF}$ regions (Fig. 1 and Fig. 2. (Grey bars)). First we studied the inter-hemispheric interaction of the somatosensory cortex using a forepaw stimulation model (Fig. 1A). During the sensory integration stimulation paradigm (as described in methods) BOLD signal in the left $S1_{FL}$ remained elevated for the entire period of right forepaw stimulation. However in the right $S1_{FL}$ there was a small but significant initial increase (▲) in the BOLD signal even in the absence of stimulation of the left forepaw. Furthermore during the subsequent 30 s stimulation on the left forepaw in the presence of the continuous (and prior) 90 s stimulation of the right forepaw, the BOLD signal in the left $S1_{FL}$ was augmented (Fig. 1B (white bar). Similar results were observed after interchanging the stimulation paradigm from right to left paw (Fig. 1C). Using whisker and forepaw stimuli on the same sides of the body (Fig. 2A), we have found that the enhancement of the BOLD response is only observed in the primary forelimb cortex when the two stimuli are added (Fig. 2C), but this enhancement with two simultaneous stimuli is not observed in $S1_{BF}$ (Fig. 2B). We are currently exploring neural recordings during this stimulation paradigm to understand the neurophysiologic basis for the sensory integration phenomenon.



REFERENCES

[1] Armstrong-James M and George MJ (1988) *Exper Brain Res.* **70**:155-165. [2] Chapin JK and Lin CS (1984) *J Comp Neurol.* **229**:199-213. [3] Meredith MA and Stein RE (1986) *J Neurophysiol.* **56**:640-642. [4] Schuler et al (2001) *J Neurosci.* **21**:5251-5261. [5] Ghazanfar AA and Schroeder CE (2006) *Trends Cog Neuro Sci.* **10**:278-285. [6] Driver J and Noesselt T (2008) *Neuron.* **57**:11-22. [7] Cauller et al (1998) *J Comp Neurol.* **390**:297-310. [8] Olavarria et al (1984) *Brain Res.* **291**:364-398. [9] Ogawa et al (2000) *Proc Natl Acad Sci.* **97**:11026-11031. [10] Sanganahalli et al (2008) *NMR Biomed.* **21**:410-416.

ACKNOWLEDGEMENTS: This work was supported by grants from NIH (MH-067528, NS-52519).