Cortical and subcortical activations by high field fMRI for different sensory stimuli

B. G. Sanganahalli[1], P. Herman[1,2], C. J. Bailey[1,3], D. L. Rothman[1,4], H. Blumenfeld[5,6], and F. Hyder[1,4]

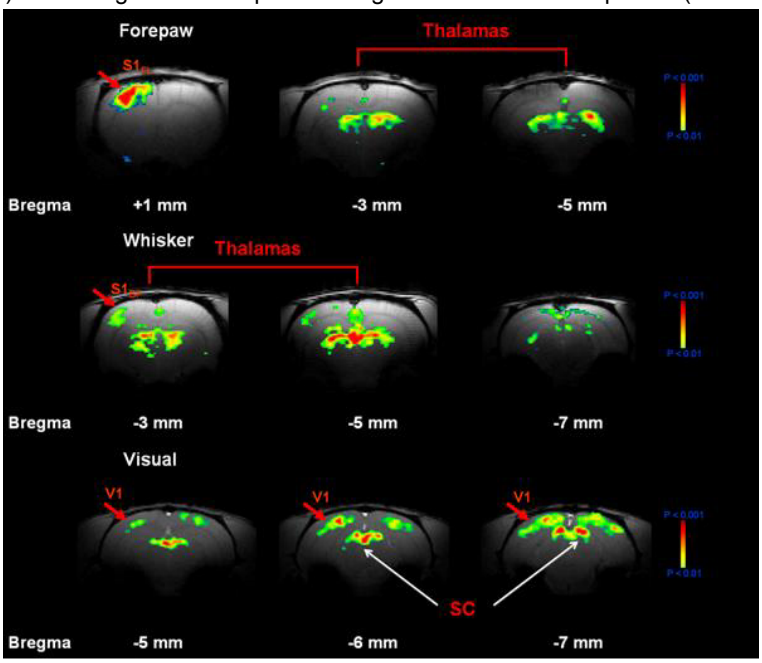
[1]Diagnostic Radiology, Yale University, New Haven, CT, United States, [2]Human Physiology, Semmelweis University, Budapest, Hungary, [3]Center of Functionally Integrative Neuroscience, Aarhus University, Denmark, [4]Biomedical Engineering, Yale University, [5]Neurology, Yale University, New Haven, CT, United States, [6]Neuroscience, Yale University

INTRODUCTION:

Different peripheral sensory signals converge onto subcortical regions (e.g., thalamus or superior colliculus) where they are known to be integrated [1-4]. Multisensory integration, evident behaviorally and neurophysiologically, refers to crossmodal influences in form of response enrichment or repression [2,5]. Given the extensive connections between the neocortex, the superior colliculus and the thalamus, many recent studies have proposed that subcortical structures integrate the senses even before the neocortex [6]. For example, the thalamus is a possible candidate considering its strong input-output connections with multiple cortical areas [7]. To study the interplay of cortical and subcortical regions for sensory processing there is need for developing calibrated fMRI of subcortical regions to allow quantitative imaging of their activity. The goal of the present work is to study subcortical mechanisms underlying dispersed cortical activations during sensory stimulation in rat brain by high field fMRI. These experiments should provide insights into understudied interactions between cortical/subcortical areas and provide a mechanistic basis to understand multisensory integration.

MATERIALS and METHODS:

Animal preparation: Sprague-Dawley rats were tracheotomized and artificially ventilated (70% N_2O, 30% O_2). During the animal preparation isoflorane (3%) 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. ***Whiskers 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 inbuilt solenoid unit (Solenoid valves, Cole-Parmer Instrument). The details of the forepaw, whisker and visual stimulation procedure are available in our previous paper [8]. **Visual Stimulus delivery**(8Hz, blue light)**:** Fiber optic cables (∅ : 1mm) were used to guide the light of two strong LEDs, placed outside the scanner room, into the eyes of the animal as it lay positioned in the imaging bore. Acrylic lenses were used to shape the beam of light exiting the cables, to facilitate accurate and reproducible placement. The intensities of the LEDs were controlled independently using Spike 2 software and μ -1401 DAC (CED, Cambridge, UK) to adjust the voltage at the input of constant current drivers. ***fMRI (n=20):*** All fMRI data were obtained on a modified 11.7T Bruker horizontal-bore spectrometer (Billerica, MA) using a ^{1}H surface coil (Ø = 1.4 cm). The images were acquired with gradient echo EPI sequence (TR/TE = 1000/15).



RESULTS and DISCUSSION:

Our results demonstrate reproducible subcortical activity during forepaw, whisker, and visual stimuli. Forepaw stimulus activates the medial portions of the laterodorsal (LD) thalamic nucleus (Fig: top row). Whisker stimulation activates broader regions within the thalamus: a small caudal part of the lateral thalamic nucleus, the dorsal and medial parts of the lateral geniculate nucleus (Fig: middle row), and small portions of the dentate gyrus. Visual stimulation activates superior colliculus (Fig. bottom row) and lateral geniculate nucleus quite robustly and even parts of the periaqueductal gray. The peak stimulation frequencies used for forepaw, whisker and visual stimuli were 3, 8, and 8 Hz respectively. Cortical BOLD responses were significantly larger as compared to the thalamic responses during forepaw and whisker stimulation. However, we found no differences in the BOLD response in cortical and superior colliculus during visual stimulation.

These results show that we can apply high field fMRI to study thalamo-cortical, colliculo-cortical, thalamo-colliculor as well as their reciprocal interactions with crossmodal sensory mixing. The three regions in the cortex represent the primary areas activated during tactile (somatosensory; $S1_{FL}$, $S1_{BF}$) and non-tactile (visual; V1) stimuli, which are connected to the subcortex (thalamus and superior colliculus, respectively). To date, however, research on multisensory integration has focused either on electrophysiology studies of individual neurons in animals or human fMRI studies investigating diffuse cortical areas involving much larger neuronal populations. Therefore these experiments should provide insights into the interactions between cortical and subcortical areas to provide a mechanistic basis for understanding multisensory integration.

REFERENCES[1] Steriade et. al (1993) Science **262** : 679-685 [2] Stein et. al (2008) Nat Rev Neurosci **9** : 255-266. [3] Laurienti et. al (2005) Exp Brain Res **166**: 289-29. [4] Senkowski et. al (2008) Trends Neurosci **31** : 401-409 [5] Stein and Meredith (1993) The Merging of the Senses, MIT Press, Cambridge, Mass [6] Ghazanfar and Schroeder (2006) Trends Cogn. Sci. **10** : 278-285. [7] Cappe et. al (2009) Hear Res (*in press*) [8] Sanganahalli et. al (2009) Methods Mol Biol **489**: 213-242.

ACKNOWLEDGEMENTS: This work was supported by grants from NIH (R01 MH-067528, P30 NS-52519).