Sensory-induced sub-cortical activations in rat brain by fMRI

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INTRODUCTION:

Cortical activations are usually interpreted to represent behavior. However function of subcortical areas can be considered to be "coupled" with activities of the cerebral cortex [1]. Sensory signals from the peripheral sensory organs cannot bypass the thalamus and/or the superior colliculus prior to their entry into the higher cortical areas. Generally, superior colliculus is important for non-tactile stimuli (e.g., visual, auditory) [2 - 4], whereas thalamus is more responsive to tactile stimuli (e.g., forepaw, whisker) [5 - 8]. Because different peripheral sensory pathways converge onto these subcortical regions, they are important sites for studying the interplay across different senses modalities [9 - 11]. Current understanding about BOLD signal and the underlying neurophysiology is based predominantly on functions of the cerebral cortex. BOLD activations of subcortical regions, in contrast, are hard to detect because of low sensitivity and/or difficult access. To study interactions between cortical and subcortical regions by fMRI, the BOLD signal in subcortex must be measured with the same level of MR sensitivity as that achieved in cortex. Thus to establish early foundations for crossmodal sensory studies, we need to measure reproducible BOLD activation patterns of thalamus and superior colliculus for different sensory paradigms in relation to the activated cortical areas.

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%) 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 [12]. **Visual Stimulus delivery**(8Hz, blue light)**:** Fibre 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:

Independent stimulation of forepaw or whisker or visual activated the contralateral $S1_{FL}$ or $S1_{BF}$ or V1 regions. Our results (Fig. 1) demonstrate reproducible thalamus and superior colliculus activity during forepaw, whisker, and visual stimuli in rats. Forepaw stimulation activates the medial portions of the laterodorsal (LD) thalamic nucleus (Fig. 1A). 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.1C), and small portions of the dentate gyrus. Visual stimulation activates superior colliculus (Fig.1E) and lateral geniculate nucleus quite robustly and even parts of the periaqueductal gray. The 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 (Fig.1B) and whisker stimulation (Fig.1D). However, we found no differences in the BOLD response in cortical and superior colliculus during visual stimulation (Fig.1F). Thus we can apply high field fMRI (high S/N ratio) 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). These results have significance in understanding the role of both cortical and subcortical areas during multisensory integration.

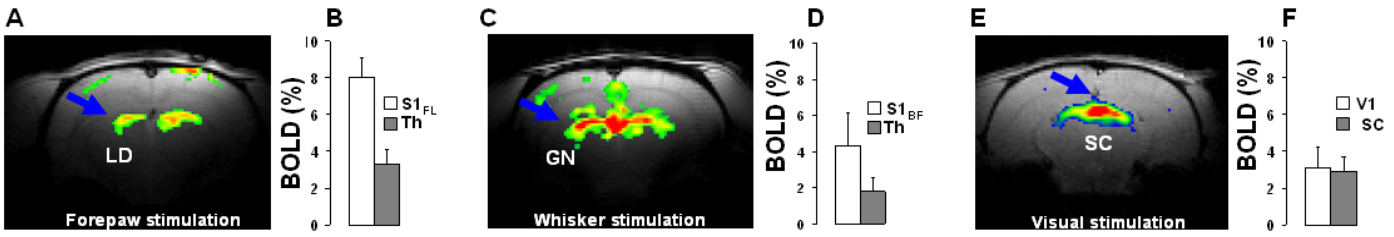

Figure 1. Subcortical BOLD activations (11.7T). Activations of thalamus and superior colliculus observed during tactile (forepaw, whisker) and non-tactile (visual) stimuli. Thalamic activations were found in (A) different parts of laterodorsal (LD) nuclei, as well as (C) medial and dorsal parts of the geniculate nucleus (GN) (E) Top three layers of the superior colliculus (SC) were reproducibly observed. The slices shown, from left to right, are from 3, 5, 6.0 mm posterior to bregma. Cortical (white) and subcortical (Grey) activations of BOLD signal are shown in Fig. 1B (forepaw), Fig.1D (whisker) and Fig.1F (visual) stimulations. fMRI data using a single run scan of a block design paradigm (stimulus duration, 30 s).

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