BOLD fMRI of the Visual System in Awake and Anesthetized Rats

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Introduction: BOLD fMRI is widely used to study the function of brain. The large majority of rodent fMRI studies, anesthesia is used to immobilize the animal. It is well known that the physiological state of brain can be altered by analgesics. Thus the scientific significance and relevance of the result obtained under analgesia may be limited. There have been some studies that fMRI was conducted on conscious rats if they were properly trained and acclimated to holding device [1,2,3,4]. In the present study, we compare the BOLD fMRI of the visual system in awake and anesthetized rats. A head post was implanted to minimize the head motion and rats were trained to accustom to a restrainer. Brain activity in response to various frequencies of flashing light was explored.

Methods: Animal experiments and training procedures were approved by the NIH Institutional Animal Care and Use Committee. In addition to alpha-chloralose anesthetized SD rats (n=4), another group (n=5) was trained for awake imaging. Those rats were trained to habituate to the restrainer and scanner noise for two weeks, and then received head post implantation. The PEEK plastic head post with a screw hole was affixed to the skull by dental cement. During head-fixation training, the rat head were secured to a restrainer by the head post. A head support was also used to minimize stress and also confine the head motion. After training, brain fMRI in response to visual stimulation was evaluated. All images were acquired with an 11.7T/31cm horizontal bore magnet (Magnex, Abingdon, UK), interfaced to an AVANCE III console (Bruker, Billerica, MA). Spin-Echo EPI was performed with the following parameters: FOV= 1.92x1.92 cm, matrix 64x64, TR= 1500 ms, TE = 35 ms, 6 slices, slice thickness = 2 mm. Visual stimulation was delivered by a white LED light bulb flashing at four frequencies (1, 4, 8, and 10 Hz). Each session consisted of 5 epochs (30s visual stimulation followed by 30s rest). Each rat received 4 sessions for each frequency. Animals were allowed to rest for few minutes between sessions. All images were aligned and analyzed by AFNI. Few images with large motion artifacts were excluded from analysis. To combine results from individual animals in the each group, a template image was derived from all rats in the group. Then all images were co-registered to the template image for further analysis.

Results: Figure 1 shows brain activity in response to 10Hz light stimulation of an awake rat. Three regions of the visual system show significant activation ($p < .001$): lateral geniculate nucleus (LGN), superior colliculus (SC) and the visual cortex (VC). The averaged time courses of signal change in center of these activated regions (4x4 voxels) are shown in the right panel. The averaged signal changes in these regions were 1.66%, 1.64%, and 0.98% respectively. Figure 2 shows the group maps of fMRI activity in response to low (1 and 4Hz) and high (8 and 10 Hz) under anesthetized or awake rats. The group maps were threshold by $p < 0.05$. In comparison to anesthetized rats, awake rats showed stronger fMRI activation in the visual system, especially to high frequencies. The LGN and SC of anesthetized rats also responded to high frequencies.

Discussions and Conclusions: To our knowledge, this is the first study showing BOLD fMRI on awake rats in response to visual stimulation. High frequencies of visual stimulation elicited more activation in the visual system. The frequency-dependent activation of SC in anesthetized rats is consistent with a previous study [5]. These findings indicate that fMRI experiments in awake rats may be more appropriate to study the function of visual system. Future studies will explore fMRI activation induced by different stimulus type in awake rats.

References: [1] King et al, J Neurosci Methods, 148:154-160 (2005). [2] Tabuchi et al, Brain Res, 951:270-279 (2002). [3] Khubchandani et al MRM, 49, 962-967 (2003). [4] Sachdev et al, NeuroImage, 19, 742-750, 2003. [5] Van Camp et al, J Neurophysiol, 95: 3164–3170, 2006.

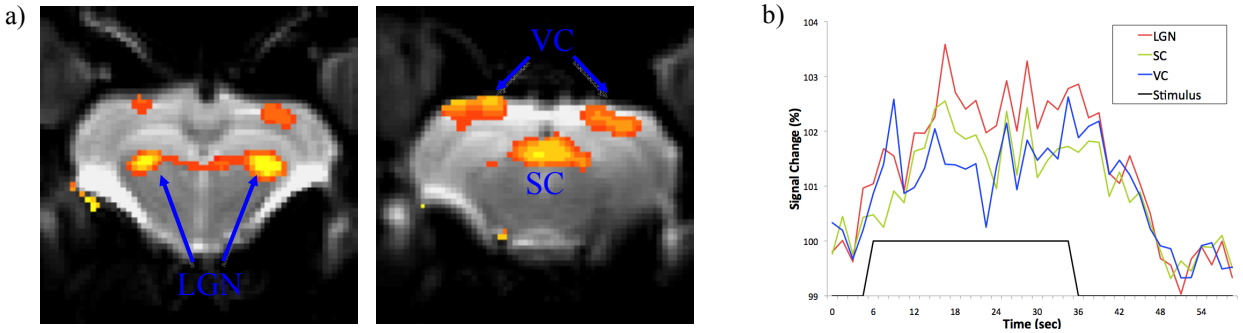

Fig 1. a) BOLD fMRI in response to 10Hz flashing light in an awake rat. b) Averaged time courses of signal change in these regions.

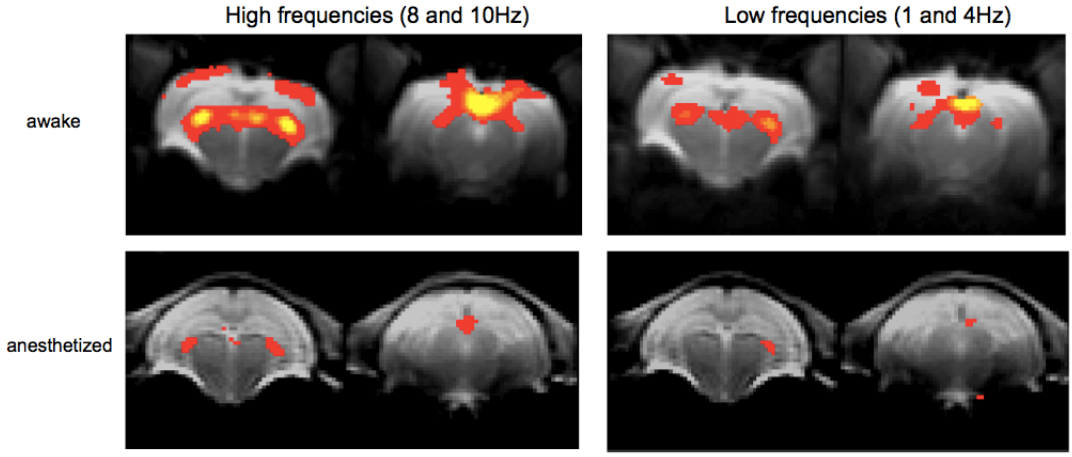

Fig 2. Group maps of fMRI activity in response to high frequencies (8 and 10 Hz, left column) and low frequencies (1 and 4Hz, right column) in awake rats (upper row) or anesthetized rats (lower row).