Study of Post-stimulus BOLD Undershoots between Lateral Geniculate Nucleus and Primary Visual Cortex in Cat Brain

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Introduction One well observed phenomenon in the fMRI study of visual stimulation in the human brain is a prolonged post-stimulus BOLD undershoot in the activated visual cortex (V1) although whether the undershoot is due to the delayed CBV or $CMRO_2$ recovery compared to that of CBF is still under debate[1-3]. It is important to examine if the same phenomena also exists in the sub-cortical lateral geniculate nuclei (LGN), which is the first stage to process the visual input receiving from retina. The unique advantages of high sensitivity and specificity of fMRI at high fields enable one to reliably map the brain activation in both small sub-cortical nuclei and cortical regions[4]. In this study, we conducted an fMRI study in cat using flicking visual stimulation to simultaneously examine the BOLD undershoots in both LGN and V1. The results indicate that the temporal BOLD changes after the cessation of visual stimulation are dissociated between V1 and LGN, and only V1 but not LGN is characterized by BOLD undershoot.

Method Cats were anesthetized with 0.9-1.2 isoflurane in a mixture of 70%N_2O/30%O_2. The fovea area of the cat retina was located with the aid of a fundus camera (Zeiss, Germany) ensuring that the cat eyes were focused on the visual stimulus. The head position of cat was fixed by a head-holder with mouth-bar and ear-bars. The visual stimulus consisted of two separate red LED boards with large view angles allowing either binocular or monocular visual stimulation at 2-8 Hz flicking frequency. All the fMRI studies were performed on a 9.4T horizontal magnet (Magnex Scientific, UK) interfaced with a Varian INOVA console (Varian Inc., Palo Alto, CA). The multiple-slice T_1-weighted anatomical images were acquired first for identifying the appropriate image slices and brain structures of the cat visual system. Then, the multi-slice and multi-segment gradient echo planar images (TE = 17.5 ms, FOV = 5×5 cm^2, 390μm×390μm in-plane resolution, 1 mm slice thickness and four adjacent coronal images) were applied for fMRI studies using a block paradigm design (4 control and 3 task periods with 8 images per period in an interleaved way). Each fMRI run consisted of three visual tasks (binocular stimulation, left and right eye monocular stimulations) in a random order. Multiple fMRI runs were performed in each cat for signal averaging. Four cats were used for BOLD-based fMRI studied. In addition, the superparamagnetic particle (MION) was used for imaging and quantifying CBV in one cat using the flicking visual stimulation between black and white screen presentations.

Results Figure 1 illustrates the high-resolution fMRI maps from two representative imaging slices acquired from a cat during the binocular visual stimulation. It shows robust brain activation located bilaterally in both LGN and V1 areas across multiple imaging slices. Figure 2 shows the BOLD time courses covering control, stimulation and post-stimulation periods during three visual stimulation tasks (one binocular and two monocular) and the averaged time course from these three tasks in LGN and V1, respectively. First, the BOLD changes in LGN were significantly larger than that in V1 for all visual tasks (near double for this cat). Second, both LGN and V1 BOLD time courses show an overshoot at the beginning of visual stimulation. Third, there is a significant and prolonged post-stimulus BOLD undershoot in the activated V1 region for all visual tasks. However, observed undershoots in V1 was absent in the activated LGNs although the hyperoxic BOLD signal of LGN during the visual stimulation is much stronger than that of V1. The same results were obtained consistently in other three cats studied using BOLD-based fMRI. Finally, the preliminary CBV results indicate similar BOLD and CBV time courses in LGN during and after a binocular visual flicking stimulation without showing a significant delay of CBV recovery.

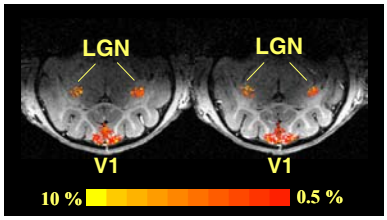

Fig. 1 Multi-slice fMRI maps cat brain during visual stimulation. LGN: lateral geniculate nucleus, V1: visual cortex.

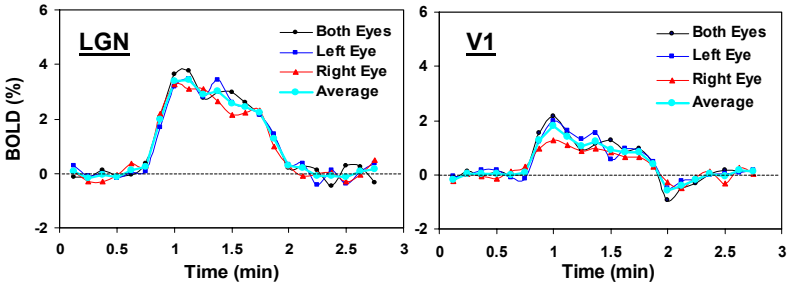

Fig. 2 BOLD time courses during binocular (both eyes), monocular (Left and right eye, respectively) visual stimulation and the average time course of these three tasks in LGN and V1 of one representative cat.

Discussion and Conclusions: During a visual stimulation, LGN receives visual inputs from retina first and then projects to V1. Thus, visual perception or stimulation must activate LGN in the thalamus and then the cortical V1 areas. Though a prolonged post-stimulus BOLD undershoot has been frequently observed in the human V1 during a visual stimulation, the origin of the undershoot related to the interplay among hemodynamics, oxidative metabolism and neuronal activity is still not fully understood. Beyond this mechanistic issue, one crucial question is whether the post-stimulus BOLD undershoot is a general phenomena in brain function, in particular, in the visual sensory system. Our results clearly reveal dissociated post-stimulus BOLD changes between V1 and LGN showing the absence of post-stimulus BOLD undershoot in LGN during the same visual stimulation in the same cat. It is likely that the discrepancy of post-stimulus BOLD behavior between LGN and V1 as observed in this study can be attributed to the distinct hemodynamic changes in LGN in response to visual stimulation. This notion was supported by our preliminary CBV observation. Our results also reveal the complexity of BOLD signal and suggest caution has to be taken when one interprets fMRI results. Currently, we are investigating whether the dissociation observed in this study is also true for other visual stimuli (e.g., grating stimulus).

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