The Spatiotemporal Characteristics of Visual Stimulus-Induced BOLD Responses in Cat Visual Areas

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Introduction Blood oxygen level dependent (BOLD) fMRI has been widely used to map the neuronal activity of the cortical visual areas in mammals. In addition, the subcortical visual regions such as lateral geniculate nucleus (LGN) have also been successfully mapped in humans (1). However, unlike visual cortex, our understanding about the spatiotemporal BOLD response induced by visual stimulus in LGN is relatively poor. In this study, we investigated the BOLD response in the cat primary visual cortex (A17) and LGN using a high spatiotemporal-resolution gradient-echo (GE) echo planar imaging (EPI) technique. We compared the dynamic properties of the BOLD response in these visual regions and correlated BOLD activation maps with venographic images.

Materials and Methods Seven adolescent cats were anesthetized with 1% isoflurane, and their physiology was kept within a normal physiological range. All MR experiments were carried out at 9.4 T with a custom-built half-volume coil placed on top of the brain. Multiple 2-mm thick coronal slices from anatomical T_1-weighted images were chosen to include LGN and A17 for fMRI studies, according to a stereotaxic atlas (2). BOLD fMRI was performed with a partial-Fourier GE EPI (TR = 1 s, TE = 20 ms, FOV = 4 x 3 cm^2, in-plane resolution=313 x 313 μm^2). Only 60 k-space lines were acquired (12 negative and 48 positive), and an iterative algorithm implemented in Matlab was used to fill in the missing 36 k-space lines (3). Venograms were acquired with 3-D RF-spoiled GE with flow compensation (TR = 50 ms, TE = 20 ms, FOV = 4 x 3 x 2 cm^3, isotropic resolution = 156 μm^3) (4). Visual stimulus of 4-s duration consisted of full-field moving gratings with spatial frequency of 0.15 cycle/degree; although temporal frequencies were 1, 2, 10, and 20 Hz (pseudo-randomized), runs with the same temporal frequency were averaged and only the 10-Hz data are displayed here. Bicubic interpolated Z-statistical images used clusters determined by $Z > 2.3$ and a cluster significance threshold of $P = 0.01$. BOLD data were linearly interpolated to 0.2-s resolution and onset times were determined as the point at which 10% of maximum response was attained for each individual animal. Activation maps were generated with FSL software, while other post-processing and data visualization were accomplished with ImageJ, MRIcroN and Stimulate, software packages.

Results and Discussion Peak amplitude of the averaged BOLD response was significantly larger for LGN vs. A17 (Fig. 1, $p < 0.0002$, paired t-test, Error Bar = 1 SD). Onset time of the visual stimulus-induced BOLD response was 2.17 ± 0.27 s (mean ± SD) for LGN and 2.66 ± 0.22 s for A17, and the difference between the two regions was significant ($p < 0.006$, paired t-test). Similar trends for LGN vs. A17 amplitudes and onset times were also observed for 1, 2 and 20-Hz temporal frequencies (data not illustrated). Since electrophysiological measurements show that onset times for LGN and A17 are 79.0 ± 8.3 ms and 113.7 ± 5.7 ms respectively (5), we expect that neural activity-induced hemodynamic responses should be faster for LGN than in A17. However, the difference in onset times of the BOLD responses for LGN vs. A17 are far larger than the timing difference of neuronal responses, indicating that neurovascular coupling and/or vasculature in these two areas are different. In comparison, human BOLD fMRI studies show no significant difference in onset times (1). Possible causes of this discrepancy include partial volume effects in human studies and species differences.

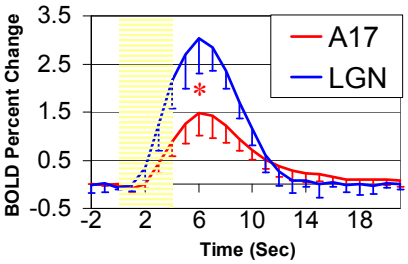

Fig 1. Average BOLD time courses for 10-Hz temporal frequency of visual stimulation. (n = 7) Yellow shading represents stimulus duration.

BOLD responses show significant activation in both cortical and subcortical visual areas. Fig. 2 shows activation maps from one representative animal overlaid on venographic data. Notably, there are BOLD response outside the LGN (e.g., Figs. 2c and 2d), which is spatially correlated with either internal cerebral veins or branches (in humans, these branches are known to drain the LGN). Hence, the contamination of draining vein is dominated at posterior part of LGN while A17 is dominated at cortical surface.

In conclusion, temporal hemodynamic responses in LGN are significantly different from A17, and the spatial distribution of responses also appears different. Caution should therefore be taken when interpreting BOLD responses for both cortical and subcortical regions.

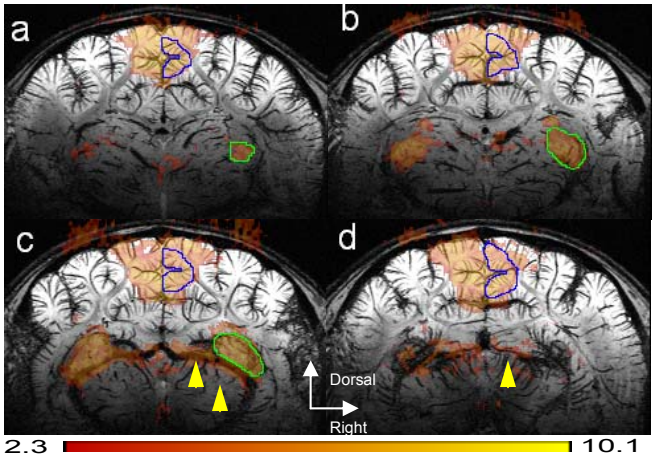

Fig 2. BOLD responses (Z-statistic maps) overlaid on minimum-intensity projection venograms for contiguous slices (anterior to posterior). Blue contours outline A17, green contours roughly indicate LGN boundaries, and yellow triangles indicate internal cerebral veins or branches which may drain the LGN on one hemisphere.

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