Detecting LGN Activation in Human Using Quantitative Perfusion-based FMRI: A Feasibility Study

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Introduction:

The lateral geniculate nucleus (LGN) of the thalamus relays visual information from the retina to the primary visual cortex. Therefore, understanding LGN function is critical to understanding human visual perception. It is difficult to study LGN function using existing brain-mapping techniques mainly because of its small size and deep sub-cortical location. Thus far, blood oxygen level dependent (BOLD) functional MRI (fMRI) is considered to be the best non-invasive approach for detecting LGN activation [1,2]. In this study, we demonstrate that perfusion-based fMRI using arterial spin labeling (ASL) MRI can also detect LGN activation in the presence of visual stimulation. As compared to BOLD-based fMRI, perfusion-based fMRI measures changes in tissue blood flow and thus may provide a more accurate assessment of the associated neuronal activity [3].

Methods:

5 healthy adult subjects with normal vision participated in the study after giving informed consent. All experiments were done on a General Electric (GE) 3.0 Tesla EXCITE system with an 8-channel array coil. Five axial slices (5mm thick) were acquired at the level of LGN and primary visual cortex. A quantitative pulsed ASL sequence (PICORE QUIPSS II) with spiral readout was used (TR 3.0 sec, TI1 700ms, TI2 1400ms, tag width 200mm, FOV 22cm, flip angle 90, matrix size 64x64, repetitions 80). Separate perfusion-only (TE=3.2msec) and perfusion/BOLD (TE =25 msec) experiments were performed on all subjects and each experiment was repeated in the same session (4 functional scans in total). In the perfusion-only experiments (TE=3.2msec), background suppression was used [4]. In the perfusion/BOLD experiments, dual echoes (TE=3.2msec and 25msec) were acquired to allow simultaneous acquisition of perfusion and BOLD weighted images. Physiological parameters (cardiac signal and respiratory effort) were collected during all functional experiments. A high-resolution structural scan (3DFSPGR) was also acquired at the end of each scan session. The visual stimulus paradigm consisted of a block design of a maximum-contrast flickering checkerboard (8Hz reversal rate) alternating between left and right visual field (30 sec on, 30 sec off, 4 cycles). Subjects were instructed to fixate at the center of the screen throughout the functional scans.

BOLD signals were obtained by averaging the control and tag images from the second echo (TE=25msec) data from the perfusion/BOLD experiments and perfusion signals were calculated from the running subtraction of control and tag images from the first echo (TE=3.2msec) data of the perfusion-only experiments. Physiological noise correction was applied to both BOLD and perfusion time courses using a modified RETROICOR method [5]. For each subject, the two repeated experiments were averaged and correlation maps were created. Based on the anatomical images, LGN was delineated and subsequently used as region of interest (ROI). A same correlation threshold of 0.4 (corresponding to $p < 10^{-4}$) and minimal cluster size of 2 were used for both BOLD and perfusion data to select activated voxels in LGN. The final BOLD and perfusion time courses were obtained from the average of the individual time courses in the activated voxels within the ROI.

Results:

Perfusion activation in LGN was detected in all 5 subjects in the background-suppressed experiments. The amplitude of perfusion activation varied from 60-140% and the activation size (number of activated voxels) was 2-4 voxels (corresponding to 118-236mm^3 total volume). There is no significant difference between left and right LGN perfusion responses ($p=0.53$). Bilateral BOLD activation was also consistently observed in all subjects, with an activation amplitude of 0.5-1% and activation size of 4-10 voxels (236-590mm^3 total volume). Figure 1 demonstrates the measured activation maps and time courses from subject 1.

Discussion:

The location of LGN from either BOLD or perfusion activation map agrees well with the high-resolution anatomical images. The activation size of perfusion response is smaller than that of BOLD response, suggesting that perfusion-based fMRI may be more localized to the neuronal activity, but also possibly reflecting the lower sensitivity of ASL. The voxel size used in this study was 3.4x3.4x5mm^3, larger than that used in the previous studies. Increasing the voxel size was necessary because perfusion-based fMRI has intrinsically lower signal-to-noise ratio (SNR) than BOLD fMRI. Experiments done with smaller voxels did not show consistent perfusion activation in all subjects. The bigger voxel size increased the partial-volume effects and might have caused underestimation of the activation amplitudes and sizes. Nevertheless, robust LGN activation was detected in all experiments and in all subjects, and the measured activated volume agrees well with the reported anatomical volume (91.1-157mm^3) [6]. Finally, we found that background suppression and physiological noise correction are necessary for studying perfusion changes in human LGN. Without background suppression and physiological noise correction, the SNR of perfusion measurement was too low to reliably discern activation in all subjects.

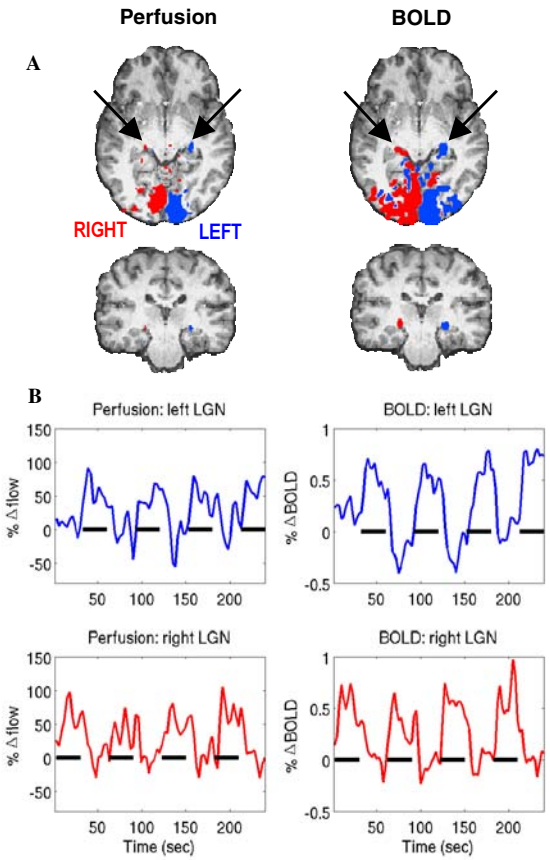

Figure 1: A. Perfusion and BOLD activation maps overlaid on top of anatomical. The arrows indicate LGN. B. Measured perfusion and BOLD time courses in left and right LGN. The black bars indicate visual stimulation.

Conclusion:

We have demonstrated that perfusion-based MRI can be used to reliably detect blood flow changes in human LGN. This method should prove to be useful for studies of human visual function in both research and clinical settings. To the authors' knowledge, this is the first quantitative perfusion-based fMRI study of LGN in humans.

Acknowledgement: This study is supported in part by NIH grant 5R01EY011008-10.

Reference:

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