Perfusion-based FMRI in Human LGN and Visual Cortex Reveals a Regional Difference in the Coupling Between Cerebral Blood Flow and BOLD

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Introduction:

The human visual pathway consists of neural projections from the retina to the lateral geniculate nuclei (LGN), and from LGN to the primary visual cortex (V1). Both V1 and LGN have been studied using blood oxygenation level dependent (BOLD) functional MRI (fMRI) [1,2,3,4,5]. The measured percentage change of the BOLD signal in LGN during activation is typically 2-3 times smaller than that in V1 [1,5]. The interpretation of such a regional difference in BOLD signal is difficult since the BOLD signal is a complex function of changes in multiple physiological parameters, such as cerebral blood flow (CBF), cerebral blood volume (CBV) and the cerebral metabolic rate of oxygen ($CMRO_2$). Perfusion-based fMRI can provide simultaneous measure of functional CBF and BOLD changes. Therefore, by using perfusion-based fMRI, we sought to better understand the origin of observed BOLD differences between human LGN and V1.

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) (Milwaukee, Wisconsin) 3.0 Tesla EXCITE system with an 8-channel array coil. For the functional experiments, five axial slices (5mm thick) were acquired at the level of LGN and primary visual cortex. A quantitative pulsed arterial spin labeling (ASL) sequence (PICORE QUIPSS II) with dual echo spiral readout was used (TR 2.5 sec, TE1=3.2msec,TE2=25msec, TI1 700ms, TI2 1400ms, tag width 200mm, FOV 22cm, flip angle 90, matrix size 64x64, repetitions 96). The dual echo approach allowed simultaneous acquisition of perfusion and BOLD weighted images in a single functional scan. Two repeated functional experiments were performed for each subject, during which physiological parameters (cardiac signal and respiratory effort) were collected. 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). The subjects were instructed to fixate at the center of the screen throughout the functional scans.

The BOLD signal was obtained by averaging the control and tag images from the second echo (TE=25msec) and the perfusion signal was calculated from the running subtraction of control and tag images from the first echo (TE=3.2msec). Physiological noise correction was applied to both BOLD and perfusion time courses using a modified RETROICOR method [6]. For each subject, the two repeated functional experiments were averaged and correlation maps were created. Region of interest (ROI) for LGN and V1 were first defined on the high-resolution anatomical image. A correlation threshold of 0.3 ($p<10^{-3}$) and minimal cluster size of 2 were then used to select activated voxels within the LGN and V1 ROIs from the perfusion data. The final perfusion time course was calculated as the average of the individual time courses in these activated voxels. The same voxels were used to calculate the average BOLD time course.

Results:

Bilateral perfusion activation was detected in both LGN and V1 in all five subjects. However, in 2 of the 5 subjects, the flow measurement in LGN gave physiological implausible percentage changes (> 200%). For the remaining 3 subjects, the percentage changes in blood flow (50-100%) were comparable in LGN and V1. There is no significant difference in the measured perfusion response of the left and right LGN, or the left and right V1 ($p = 0.4$). The average percentage change of BOLD in LGN across all 5 subjects is 1%, and it is 3% in V1. The difference between the two agrees well with the previous studies. Figure 1 shows (A) the perfusion activation map and (B) the average BOLD/flow time courses measured in LGN and V1 from subject 1.

Discussion:

The BOLD signal depends on the baseline deoxyhemoglobin content (M), changes in CBF and changes in $CMRO_2$ [7]. M is in turn a function of baseline CBV [7]. Because our experiments showed similar CBF changes in LGN and V1 during activation, the observed regional differences in the BOLD response most likely reflect regional differences in M and functional $CMRO_2$ changes. The possible hypotheses are therefore: 1. V1 has a larger M than LGN, resulting in a bigger BOLD signal increase with functional activation. 2. For the same percent increase in CBF, the percent $CMRO_2$ increase is less in V1, leading to a larger BOLD signal in V1. We calculated baseline T2* values using the dual-echo data as a rough measure of M values but did not find a significant difference between T2* values in LGN and V1 ($p = 0.54$). This suggests that the difference in BOLD signal is most likely caused by a difference in the coupling between CBF and $CMRO_2$ in LGN and V1 (hypothesis 2). Although prior studies [8] suggest a close-to-linear relationship between percent changes in CBF and $CMRO_2$, little information is available on the variation of this relationship across different brain regions. Thus, additional experiments are required, in which quantitative ASL MRI is used to measure CBF and BOLD changes with hypercapnia and visual stimulation. From these experiments, regional differences in M and in the coupling between CBF and $CMRO_2$ can be more definitively determined.

Conclusion:

Perfusion-based MRI has the advantage of measuring blood flow and BOLD changes simultaneously, allowing us to further investigate the observed difference in the BOLD response between LGN and V1. Our results suggest that this difference may reflect a regional dependence of the coupling between CBF and $CMRO_2$. Additional experiments are required to test this hypothesis. Finally, the comparable CBF percentage changes measured in LGN and V1 may indicate that CBF is a more accurate reflection of neuronal activity than BOLD.

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

Reference:

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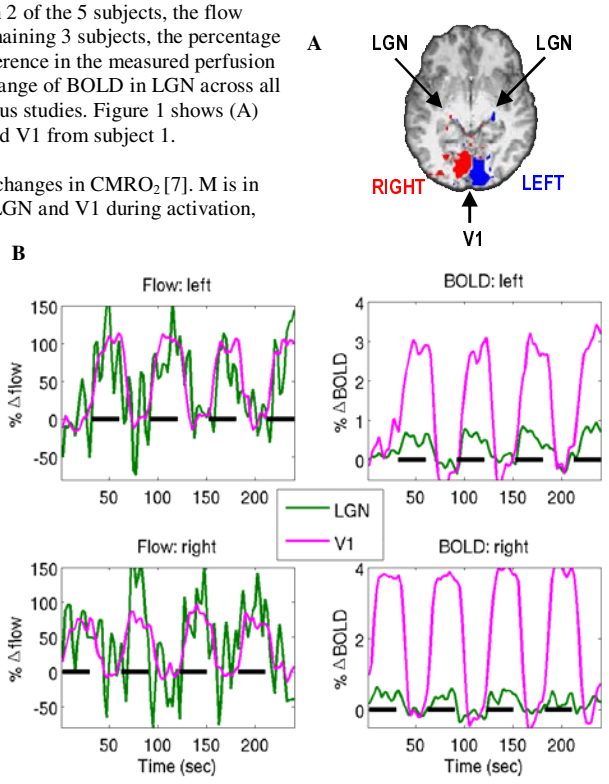

Figure 1. A. Perfusion activation map overlaid on top of a anatomical image to illustrate activation of lateral geniculate nucleus (LGN) and primary visual cortex (V1). The blue and red colors indicate a half cycle phase shift between the left and right responses, which is due to the same shift in the stimulus. B. Flow and BOLD time courses measured in LGN and V1. The black bars indicate visual stimulation.