Positive and negative BOLD and CBF responses across the early visual cortices

Rebecca J. Williams[1], Erin L. Mazerolle[1], M. Ethan MacDonald[1], Wen-Ming Luh[2] & G. Bruce Pike[1]

[1]Department of Radiology and Hotchkiss Brain Institute, University of Calgary, Calgary, Alberta, Canada

[2]Cornell MRI Facility, Cornell University, Ithaca, New York, USA

INTRODUCTION

- The negative BOLD response (NBR) has been observed across multiple brain regions, and appears to have a neuronal origin[1]
- The physiological underpinnings of the NBR are unclear
- Vasculature response differences and spatial variability between the NBR and positive BOLD response (PBR) indicates that the hemodynamic mechanisms regulating the NBR might be different from those underlying the PBR[2,3]
- The aim of the current work was to characterize CBF and BOLD signal changes across multiple visual regions, to gain a more complete understanding of the spatial variability in hemodynamic processes associated with the NBR and PBR

METHODS

Participants

- N = 5, mean age = 25.4 (± 6.3), male = 2

Data Acquisition

- 3 T GE Discovery 750, 12 channel head coil
- Dual-echo pseudo-continuous arterial spin labeling was used for simultaneous BOLD and CBF acquisition (for NBR and PBR runs)
- High resolution (2 x 2 x 2 mm) T_2*-weighted images sensitized to BOLD contrast, posterior coverage only for retinotopic mapping
- High resolution (1 x 1 x 1 mm) 3D T_1-weighted anatomical image

Stimulus paradigm

- NBRs and PBRs induced across the visual cortices using a small and large checkerboard paradigm[2] (Figure 1)
- Phase-encoded retinotopic mapping performed using standard travelling-wave rotating wedge and expanding ring paradigms[4]
- For both the NBR/PBR and retinotopic mapping paradigms, central fixation and alertness was monitored through a central fixation task and an in-scanner eye camera

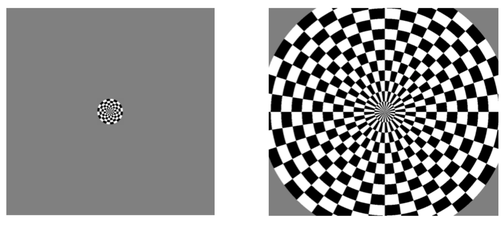

Figure 1. A small (left) and a large (right) contrast-reversing checkerboard (7.5 Hz) was presented in 6 minute runs to induce NBRs and PBRs respectively. The small checkerboard extended 3° visual angle and was expected to induce NBRs in cortical regions peripheral to fovea representation. The large checkerboard was expected to induce PBRs across the entire visual cortex. Each checkerboard was presented in 42 s blocks, interspersed with a 42 s baseline condition (blank grey screen). A central fixation dot was consistently present.

RESULTS

Retinotopic mapping and NBR/PBR activation maps

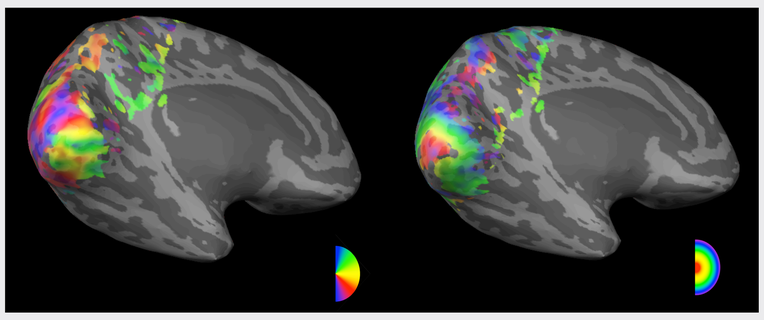

Figure 3. Representative polar angle (left) and eccentricity (right) maps from a single subject. Borders between areas V1, V2d, V2v, V3d and V3v were manually delineated from inflated hemispheres for each individual participant. ROIs for calculation of % signal change were created from all BOLD activated voxels falling within each visual field, for both NBR and PBR contrasts (see Figure 4).

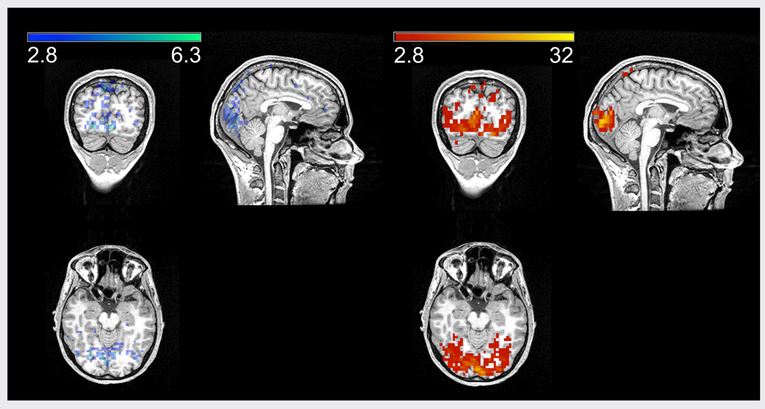

Figure 4. Contrasts for small checkerboard < baseline (NBR, left) and large checkerboard > baseline (PBR, right). Robust NBRs and PBRs were detected for most participants. SPMs thresholded $P < .05$ FDR-corrected for multiple comparisons. Colour scale indicated *t*-values. BOLD SPMs shown only. Maps are from a single representative subject.

BOLD and CBF responses across the visual regions

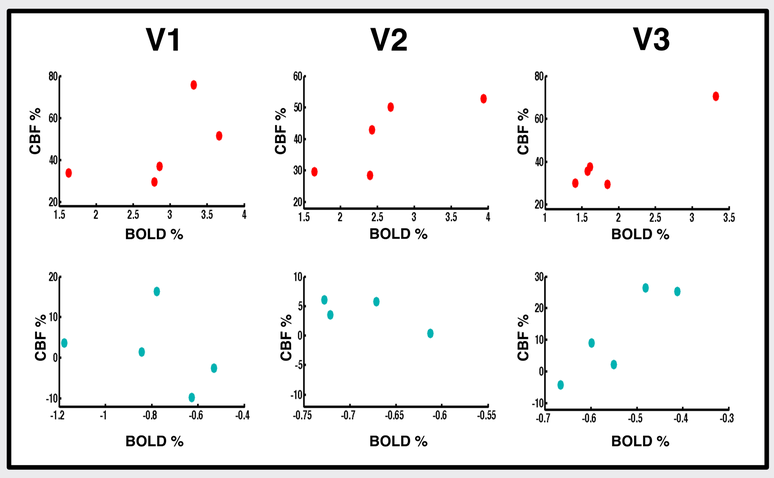

Figure 5. Scatter plots show relationship between CBF and BOLD % signal change for PBR (top, red) and NBR (lower, green) across areas V1, V2 and V3. Results are averaged across dorsal and ventral regions for V2 and V3 for each subject. A significant linear relationship was found for V3, both for the PBR (r = 0.95, $P = 0.01$) and NBR (r = 0.90, $P = 0.04$).

		V1	V2d	V2v	V3d	V3v
PBR						
	BOLD%	2.85 (± 0.77)	2.56 (± 1.16)	2.67 (± 0.71)	2.25 (± 1.23)	1.65 (± 0.50)
	CBF%	45.54 (± 18.85)	47.08 (± 17.42)	35.96 (± 6.34)	33.78 (± 3.44)	41.06 (± 17.15)
NBR						
	BOLD%	-0.79 (± 0.25)	-0.79 (± 0.17)	-0.56 (± 0.11)	-0.52 (± 0.04)	-0.56 (± 0.22)
	CBF%	1.84 (± 9.57)	-3.97 (± 8.75)	4.57 (± 8.96)	11.81 (± 14.65)	2.41 (+ 3.38)

Table 1. Mean percent signal change (with standard deviations in parentheses) across all activated voxels within each visual field. Similar response patterns were observed across the visual regions for CBF and BOLD in PBR regions. V1 and V2d saw the largest positive responses. CBF changes associated with the NBR were minimal and varied across participants, as demonstrated by the large standard deviations. **The only visual area to consistently demonstrate CBF decreases in NBR regions was V2d.**

METHODS

Data Analysis

- Dual-echo data processed using MATLAB. SPM12 and the ASL toolbox[5]
- Retinotopic maps produced in FreeSurfer to create visual field region-of-interests (ROIs) (Figure 2)

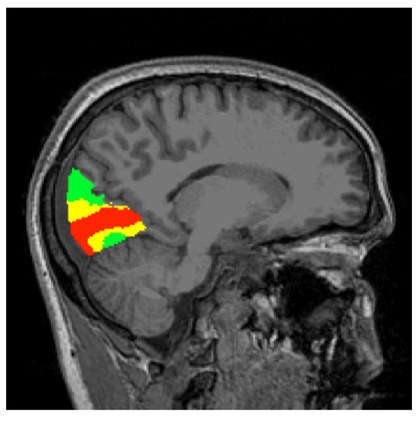

Figure 2. Area V1 in red, dorsal V2 (V2d) and ventral V2 (V2v) in yellow and dorsal V3 (V3d) and ventral V3 (V3v) in green were manually delineated from retinotopic maps to create visual field ROIs. Percent signal change within each visual region corresponding to PBR and NBR conditions were calculated for both the CBF and BOLD-weighted images.

CONCLUSIONS

- Positive CBF and BOLD changes were consistently found in PBR regions, however negative CBF changes were not always evident in NBR regions
- Negative BOLD signal changes were found across all visual regions, but CBF decreases in NBR regions were consistently found in V2d only
- Area V3 showed a linear relationship between CBF and BOLD for both PBR and NBR signal changes, however the small sample size must be considered when interpreting these findings
- These findings suggest that different physiological mechanisms may be associated with the PBR and NBR

REFERENCES

[1] Shmuel et al. *Nat Neurosci* 9: 569-77. [2] Huber et al. *NeuroImage* 15: 349-62. [3] Goense et al. *Neuron* 76: 629:39. [4] Warnking et al. *NeuroImage* 17: 1665-83. [5] Wang et al. *MRI* 26: 261-9.

Contact Information:

Dr. Rebecca Williams

Email: rjwillia@ucalgary.ca