Flow and metabolic coupling associated with positive and negative BOLD responses across retinotopic early visual cortices

Authors Rebecca J. Williams, Erin L. Mazerolle, M. Ethan MacDonald, Avery J.L. Berman, Wen-Ming Luh and G. Bruce Pike (***Correspondence and presenting author:*** rjwillia@ucalgary.ca)

Introduction Recent focus has been placed on understanding the negative BOLD response (NBR) as this may allow for functional mapping of inhibitory neural mechanisms. Currently, the physiological origins of the NBR are not entirely known, and recent research has raised the question of whether neurovascular coupling is different between the standard positive BOLD response (PBR) and NBR. An unaddressed question is whether coupling for NBRs induced by the same task differs across cortical region, which has implications for work describing the physiological origins of the NBR as well as fMRI studies using the NBR as a proxy of neural inhibition. To address this, the present study characterised BOLD, cerebral blood flow (CBF), and cerebral metabolic rate of oxygen ($CMRO_2$) changes associated with visual stimulation tasks inducing NBRs and PBRs across the early visual regions, V1, V2, V3, with the dorsal (V2d, V3d) and ventral (V3v, V3v) regions separately assessed.

Methods 11 healthy subjects (5 female) with a mean age of 25.2 years (± 4.5) were scanned. Retinotopic mapping was performed using standard BOLD acquisition, travelling-wave stimuli and FreeSurfer analysis for the delineation of the visual cortices V1, V2 and V3. A dual-echo pseudo-continuous arterial spin labelling echo planar imaging sequence was used to identify BOLD and CBF changes associated with PBRs and NBRs across the visual regions to flashing checkerboard stimuli, and a 5% CO_2 hypercapnic challenge. PBRs and NBRs from the same voxels, within each visual region (as determined from retinotopic mapping), were identified. The hypercapnia data and Davis model[1] were implemented to calculate subject and region-specific *M* values and task-related $CMRO_2$ changes. Linear regression analyses were performed on the CBF and $CMRO_2$ percent changes to determine the $CMRO_2$:CBF coupling ratio during the NBR and PBR.

Results Table 1 shows M values (%), percent signal changes and slopes of $CMRO_2$:CBF regression analyses. Linear fits shown in Figure 1.

Table 1. *For all five assessed visual regions, mean M, BOLD, CBF and $CMRO_2$ percent signal changes with standard deviations shown in parentheses. Bottom row shows slopes of $CMRO_2$ vs. CBF linear fits with R^2 in parentheses.*

	V1		**V2d**		**V2v**		**V3d**		**V3v**	
	PBR	*NBR*	*PBR*	*NBR*	*PBR*	*NBR*	*PBR*	*NBR*	*PBR*	*NBR*
M	10.10 (± 3.88)		7.22 (±2.10)		9.68 (±2.56)		6.84 (±2.11)		8.89 (±3.80)	
Δ%BOLD	2.38 (±0.44)	-0.46 (±0.23)	1.33 (±0.50)	-0.38 (±0.13)	2.10 (±0.49)	-0.49 (±0.21)	0.92 (±0.39)	-0.27 (±0.11)	1.18 (±0.53)	-0.42 (±0.20)
Δ%CBF	37.24 (±8.90)	-9.08 (±6.33)	36.04 (± 12.69)	-12.94 (± 7.86)	36.20 (±13.68)	-5.36 (±7.02)	31.03 (±12.24)	-8.44 (±11.40)	23.67 (±13.02)	-6.14 (±7.29)
Δ%$CMRO_2$	5.72 (±7.37)	-4.73 (±5.73)	15.82 (±6.91)	-8.54 (±7.04)	7.81 (±7.67)	-1.08 (±5.60)	16.36 (±7.84)	-5.31 (±9.83)	8.48 (±7.42)	-2.03 (±5.47)
$CMRO_2$:CBF	0.11 (0.02)	0.97 (0.93)	0.40 (0.53)	0.92 (0.97)	0.34 (0.36)	0.77 (0.92)	0.59 (0.83)	0.86 (0.99)	0.37 (0.38)	0.74 (0.94)

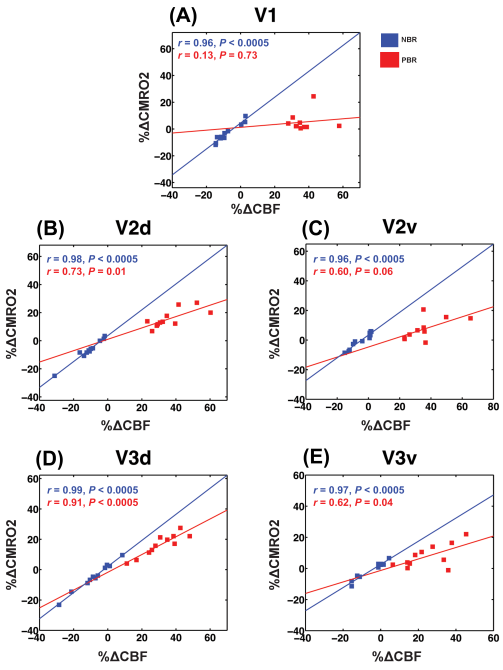

Figure 1 (right)*. Hemo-metabolic coupling associated with the NBR (blue) and PBR (red) across the five visual regions. Each data point represents a single subject.*

Discussion The $CMRO_2$:CBF coupling ratios for the NBR were closer to 1, indicating highly proportional CBF and $CMRO_2$ changes. This was consistent across all 5 assessed visual regions. Conversely, the PBR demonstrated significant variability across regions, with the difference between CBF and $CMRO_2$ changes greatest in V1. These findings may indicate different neurovascular coupling mechanisms between the PBR and NBR.

References [1]Davis, T., Kwong, K., Weisskoff, R., Rosen, B. (1998). Proc. Natl. Acad. Sci. USA, 95, 1834-39.