Highly conserved CBF/CMRO2 coupling in human primary visual cortex for chromatic and luminance stimuli

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Introduction

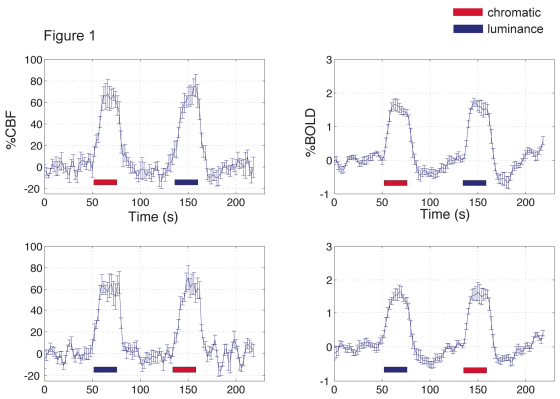
The coupling of cerebral blood flow (CBF) and the cerebral rate of oxygen metabolism ($CMRO_2$) during activation can be characterized by a single variable *n*, defined as the ratio between the fractional CBF change and the fractional $CMRO_2$ change. Knowledge of *n* is critical for any quantitative interpretation of the BOLD-effect and heavily influences the sensitivity of the BOLD-effect in detecting underlying CBF changes [1]. The calibrated-BOLD technique makes it possible to determine *n* through an indirect measurement of $CMRO_2$ [2]. The visual cortex provides an interesting test bed for examining the effects of different stimulus types on CBF/$CMRO_2$ coupling because of the observed non-uniform distribution of cytochrome oxidase (CO) in primate visual cortex (V1 and V2). CO, the enzyme that catalyzes the final transfer of electrons to O_2 in the mitochondria, exhibits a regular pattern of so-called 'blobs' in area V1 and stripes in V2 [3]. Hoge et al exploited this unique test-bed and found no differences in CBF-$CMRO_2$ coupling [4]. However, in light of results from our recent studies of potential biases in the calibrated-BOLD method, it would be important to revisit these experiments with a new experimental design [5]. In this study we measured CBF and BOLD changes in area V1 under separate conditions that preferentially drive the blob neurons with chromatic (red/green) stimuli while maintaining constant luminance, or drive the inter-blob neurons with stimuli that alternate luminance (black/white) with no chromatic information. We conducted a systematic set of experiments designed to optimize the sensitivity for detecting a difference in CBF/$CMRO_2$ coupling to critically test the hypothesis of uniform coupling. An important prerequisite to our experimental design is that the CBF change induced by both types of stimuli be approximately equal so that a measured difference in the BOLD-response would reflect a difference in the coupling of CBF to $CMRO_2$.

Methods

Seven healthy subjects were recruited and scanned according to the guidelines of the UCSD IRB. All subjects underwent a preliminary scan session in which standard stimuli for retinotopic mapping were shown and area V1 was delineated [6]. Each scan session consisted of six functional runs plus one high-resolution anatomical scan (fspgr). Runs were comprised of an initial 60s second period where subjects viewed an isoluminant gray screen, one 24s isoluminant chromatic (red/green) block, one 24s luminance-driven stimulus (black/white) block, and a 60s resting tail period (isoluminant gray screen). The RGB value for the red color was held constant for all subjects (255), and the RGB value of the green color was determined for each subject to match the luminance of the red color in a separate flicker fusion experiment to account for each subject's unique perceived isoluminance. The black/white contrast of the luminance stimuli was determined from a preliminary set of experiments to estimate what black/white contrast is needed to match the CBF change in response to the color stimulus. Each stimulus block was generated from sub-blocks consisting of simultaneous rotational (clockwise and anti-clockwise) and back and forth movement along a radial axis, switching every 1.0 – 2.5 s in a random fashion (to reduce the effect of adaptation). The switching pattern, however, was identical within in each run between the color and luminance stimuli. The spatial and temporal parameters were identical for color and luminance stimuli, with spatial frequency changing linearly from 2.5 cycles/degree in the fovea to 1.0 cycles/degree at 10 degrees eccentricity, and with drifting temporal frequency of 2 Hz. The first stimulus type (luminance or color) in each run alternated from run-to-run and from subject-to-subject to reduce biases associated with adaptation and data normalization. For all combined BOLD/ASL studies a QUIPSSII/PICORE [7] pulse sequence was used with TR=2000ms, TI_1=600ms, TI_2=1500ms, TE_1=9.4ms, TE_2=30ms, tag thickness=10cm, 4 oblique slices centered on the calcarine sulcus, in-plane resolution 2.68x2.68mm and slice thickness of 7mm. Small bipolar crusher gradients were applied to ASL runs to remove to remove signal from large vessels (b=2 s/mm^2). Additionally, pulse waveforms and respiratory motions were recorded and algorithms for physiological noise reductions were applied [8]. An ROI was constructed by averaging the CBF response data across all runs and selecting only CBF-activated voxels in V1 that exceeded a correlation coefficient of r=0.5 [5]. Runs beginning with the blob stimulus and inter-blob stimulus were averaged separately and normalized by the initial 60s rest period.

Results

Figure 1 demonstrates average (±SE) CBF and BOLD response curves for runs beginning with the chromatic stimulus (upper 2 plots) and runs beginning with the luminance (lower 2 plots) stimulus. The average CBF response generated from the color stimulus was nearly identical to the one generated from the luminance stimulus (65.4±21.1 and 64.6±20.5%, respectively). Maximal black/white contrast centered around a mean gray RGB value of 99 was needed to achieve this (±99). Associated BOLD-responses were also nearly identical to both types of stimuli (1.57±0.42 and 1.59±0.37% for chromatic and luminance stimuli, respectively). A separate CO_2 experiment to calibrate the BOLD signal was not necessary to draw conclusions about differences in CBF-$CMRO_2$ coupling since the same ROI was used to measure BOLD and CBF responses to both types of stimuli.



Conclusion

The CBF-$CMRO_2$ coupling ratio *n* in area V1 was very similar for the chromatic and luminance stimuli used, suggesting a consistent coupling for blob and inter-blob neuronal populations despite the differences in CO concentration. However, another possibility is that the observed responses, in part, reflect neuronal sensitivity to the stimulus changes within the blocks, and further studies are required to assess this potential effect.

References: [1] BM Ances et al., NeuroImage (accepted); [2] TL Davis et al., Proc.Natl.Acad.sic, USA 95:1834-9; [3] M Wong-Riley, Brain Res 171:11-28; [4] RD Hoge et al., NeuroImage 9:573-85; [5] O Leontiev et al., NeuroImage 36:1110-22; [6] SA Engel et al., Nature 369:370; [7] EC Wong et al., MRM 39:702-8; [8] K Restom et al., NeuroImage 31:1104-15.