Adaptation of cerebral blood flow and oxygen metabolsim and modulation of neurovascular coupling with prolonged stimulation in human visual cortex

Farshad Moradi[1], and Richard B Buxton[1]
[1]*Radiology, Univeristy of California, San Diego, San Diego, California, United States*

Purpose: Determine whether adaptation affects the coupling of blood flow and oxygen metabolism changes in human visual cortex.

Background: Adaptation of neural activity in sensory cortices is suggested to underlie the non-linear dynamics of BOLD response. However, the physiological mechanisms underlying adaptation of metabolic and hemodynamic activity in the brain are not well understood. We recently showed that top-down input to early sensory areas can affect the coupling between metabolic and hemodynamic activity[1]. We now examine whether the interplay between blood flow and oxygen metabolism changes is affected by intrinsic processing within the visual cortex.

Methods: A multi-pulse pseudo-continuous arterial spin labeling sequence (Optimized-MP PCASL[2], TR=3.5 s, 1600 ms tag duration at the level of internal carotid and vertebral arteries, 1400 ms post labeling delay) with a dual-echo gradient echo (GRE) spiral readout (TE_1=3.2 ms, TE_2=32ms, flip angle 90°, FOV 24 cm, matrix 64 × 64, eight 7-mm slices with 0.5 mm gap centered around the Calcarine sulcus) was used to simultaneously acquire cerebral blood flow (CBF) and BOLD in a 3.0T scanner. Six volunteers (age 25-37, 2 females) viewed peripheral radial checkerboards, at either 10% or 80% of the maximal display contrast, flickering at 3 Hz. Subjects were instructed to fixate at the center of the screen and perform a one-back memory task on digits appearing at fixation to control attention during the whole run. The peripheral stimulus was presented either continuously for 45.5 s (13 TRs), or intermittently as three epochs of 7.853 s on and off duration (Figure 1). A linear system's response to the continuous input should be equal to the sum of the original response to the intermittent input and a version of that response shifted by 7.583 s. Each subject performed four low-contrast and 2-4 high-contrast runs. The order of presentation was counter-balanced. Voxels corresponding to the position of the peripheral stimuli were identified and the flow, BOLD and metabolic responses were summed over the region of interest. Adaptation index was quantified as the difference of non-adapted (intermittent response) and adapted (continuous response divided by two) conditions, divided by the average activity.

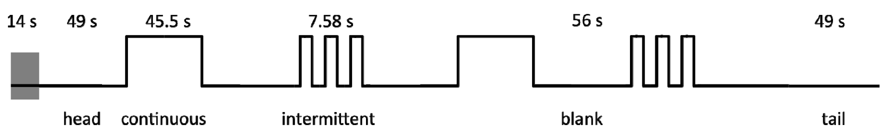

Figure 1. Stimulation paradigm. Data collected during head and tail was used for normalization.

Results: Blood flow response to peripheral stimulus showed significant adaptation (AI_{Flow}=25±3.6%/26.2±4.8%, mean±SEM for the low and high contrast stimulus, respectively (p<.001). Adaptation of the BOLD signal, however, did not reach statistical significance (AI_{BOLD}=12±9.5%/16±9.3%, p>.14). Oxygen metabolism demonstrated even stronger adaptation than flow (AI_{CMRO2}>64±0.3%). The neurovascular coupling ratio (defined as $n = \Delta CBF/\Delta CMRO_2$), was higher for the continuous stimulation than intermittent stimulation (p<.05 for both contrasts).

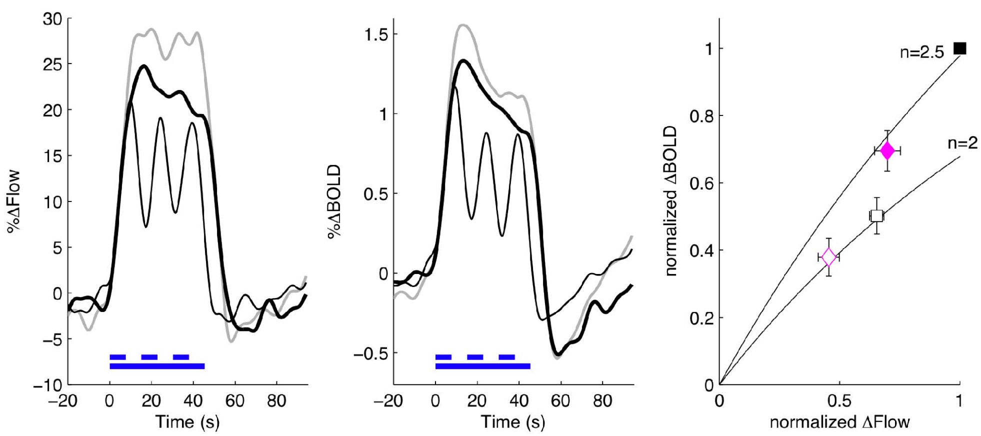

*Figure 2. Flow (left) and BOLD (middle) responses to intermittent (thin black curve) and continuous (**thick**) low contrast peripheral stimulation. The expected linear system response to continuous stimulation (gray) is depicted for comparison. Right: BOLD versus flow changes (normalized to the high contrast continuous response). Theoretical BOLD vs. Flow curves [3] for two fixed neurovascular coupling ratios are plotted for comparison. If the neurovascular coupling remains constant all points would lie on the same curve. Red: low contrast, **black**: high contrast, solid symbols: continuous, open symbols: intermittent. Error bars depict SEM across observers.*

Discussion: After prolonged stimulation, the flow and metabolic activity in the visual cortex undergo significant reduction due to adaptation. Note that the time scale of adaptation in the present study is longer (by an order of magnitude) than previously published results [4,5]. At least for the low contrast condition, these effects are not explained by saturation of the flow or metabolic responses. Since BOLD signal is a sub-linear function of flow and metabolism (for a constant neurovascular coupling), we expected an even greater non-linearity in the BOLD response. However, the BOLD signal did not show a significant adaptation non-linearity due to the changes in flow/metabolism coupling opposing the effect of flow adaptation (Figure 2). The lower coupling ratio for intermittent versus continuous stimulation may indicate adaptive mechanisms and/or decoupling of flow and metabolism during inter-stimulus intervals. Our results demonstrate that the coupling between flow and oxygen metabolism in human visual cortex is not fixed, and not only varies with top down input and attentional state of the subject [1] and contrast of the display [6], but also depends on the structure of the stimulus (continuous versus intermittent) and sensory adaptation.

Acknowledgment: NIHT32-EB005970, NS-36722, and UCSD Center for Functional MRI.

References:

[1] Moradi & Buxton. Neuroimage. 2012 Jan 2;59(1):601-7.
[2] Jung et al. Proc. Intl. Soc. Mag. Reson. Med. 17: 1578 (2009).
[3] Davis TL, Kwong KK, Weisskoff RM, Rosen BR. Proc Natl Acad Sci U S A. 1998 Feb 17;95(4):1834-9.
[4] Yeşilyurt B, Uğurbil K, Uludağ K. Magn Reson Imaging. 2008 Sep;26(7):853-62.
[5] Gu H, Stein EA, Yang Y. Magn Reson Imaging. 2005 Nov;23(9):921-8.
[6] Liang J et al. ISMRM 2009.