The ratio of CBF to $CMRO_2$ Change with Brain Activation Remains Unchanged Between Simple and Complex Stimuli in the Human Visual Cortex

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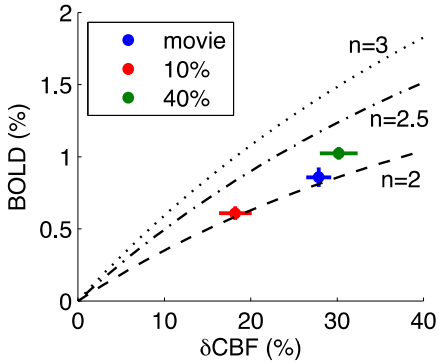
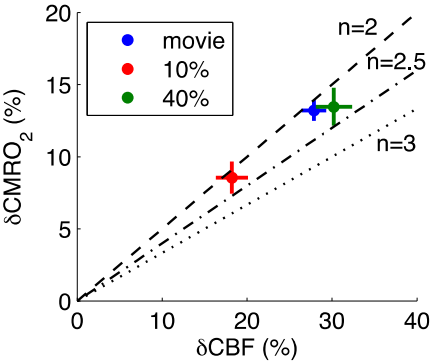
Purpose: Functional magnetic resonance imaging (fMRI) based on the blood oxygenation level dependent (BOLD) signal is a useful tool for mapping brain activation, but a quantitative interpretation of the magnitude of the BOLD response remains an obstacle to further application of fMRI to clinical problems. The BOLD signal is mostly driven by the combined changes of cerebral blood flow (CBF) and the cerebral metabolic rate of oxygen consumption ($CMRO_2$). The signal is strongly modulated by *n*, the ratio of the fractional change in CBF to the fractional change in $CMRO_2$. Numerous studies have found significant regional variation of *n* across the brain [1,2], within the same brain region, for different levels of stimuli [3,4], and with or without attention [5], but these studies all use contrived stimuli not encountered in daily life. We used a calibrated BOLD method to test whether *n* varies with the type of stimulus, either a flickering checkerboard at 10-40% contrast or a movie clip, which is a more complex and engaging stimulus compared to the simple flickering checkerboard.

Methods: Seven healthy adult subjects were studied using a dual-echo spiral arterial spin labeling (ASL) method (single-shot PICORE-QUIPSS II [6]) providing simultaneous measurements of CBF and BOLD responses. Responses were measured across three runs, which interspersed two contrast levels of an 8 Hz flickering radial checkerboard (10% and 40%) and brief movie clips from Earth: The Biography. Gamma correction of the projector was performed after measuring its luminance with a photometer, and the background gray level was adjusted to avoid any change in the overall luminance between the task and control conditions. Stimuli were presented in 20s blocks with 55s of neutral gray between blocks. Three runs were collected during each scan and subjects were scanned twice. Each stimulus type was presented a total of four times per scanning session. Functional localizer scans were also collected for each subject in which 20s blocks of neutral gray were interspersed between 20s blocks of 100% contrast 8 Hz flickering checkerboards alternating with 20s movie clips. To select a region of interest (ROI) for averaging in each subject, activation patterns in the CBF response to the functional localizer were found using a general linear model approach. ROI-averaged time courses for the BOLD and CBF signals were constructed for the three stimulus types. The corresponding $CMRO_2$ time course for each stimulus type was calculated using the Davis model [7]. We used an assumed value of the scaling parameter *M* (10.6% corrected for TE) based on our previous studies with similar methods and analysis in which *M* was measured [8,9]. We tested the significance of this assumption by repeating the calculations for different values of *M* over a range (9-12%) consistent with what we have found with hypercapnia calibration under similar experimental conditions.

Results: Neither the BOLD response nor the CBF response to the movie stimulus was statistically different than the responses to the 40% contrast flickering checkerboard (p=0.15 and p=0.53 respectively). Additionally, the calculated $CMRO_2$ response does not appear to be different between these two stimuli (p=0.89). These findings imply that the CBF-$CMRO_2$ coupling between the flickering checkerboards and the more complex movie stimulus are not significantly different, which was in fact the case: movie n=1.9±0.31 vs. 10% n=2.1±0.30, p=0.57 and movie vs. 40% n=2.4±0.24, p=0.09). Over the range of *M* examined, lower *M* tended to increase all values of *n* slightly while higher *M* decreased *n*. Our conclusions regarding the similarity of the 40% contrast response and movie response remain the same over this range.





Conclusions: All calibrated-BOLD studies to date have explored the effects of simple stimuli such as a flickering checkerboard and have found uncoupling of CBF and $CMRO_2$ [1-4]. Here, we explored whether a more complex stimulus would lead to different coupling or uncoupling of CBF and $CMRO_2$. We postulated that the visual cortex response to a movie could be affected by inputs from other areas of the brain not being driven by the simple checkerboard stimulus, perhaps through a similar mechanism by which modifying attention can affect coupling [5]. We found this was not the case, and the visual cortex appears to respond in a similar fashion to a flickering checkerboard and a complex movie with responses to the 10% and 40% contrast levels bracketing the response to the movie stimulus. This validates using simple stimuli like flickering checkerboards in place of more complicated everyday stimuli and vice versa in order to study the visual cortex response.

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