Differences in neurovascular coupling in areas with positive and negative BOLD signal

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Introduction

While the dynamics and mechanism of the positive BOLD response have been well studied, much less is known about the mechanism of the negative BOLD response. Although the negative BOLD response is related to decreases in neural activity [1] and in CBF [2], the temporal dynamics differ from that of the positive BOLD signal [1]. Here, we studied the properties of the negative BOLD response in greater detail by comparing the BOLD-, functional CBV- and CBF- responses in regions exhibiting positive and negative BOLD in primary visual cortex (V1) of anesthetized monkeys.

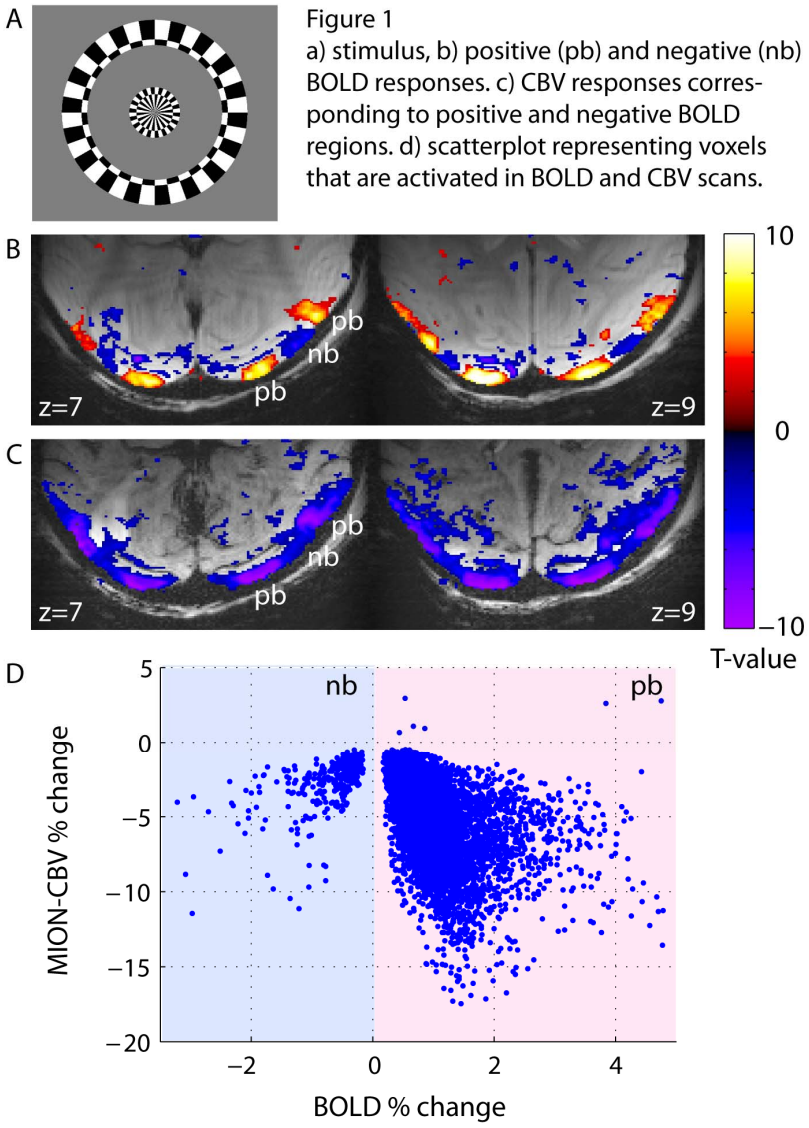

Figure 1
a) stimulus, b) positive (pb) and negative (nb) BOLD responses. c) CBV responses corresponding to positive and negative BOLD regions. d) scatterplot representing voxels that are activated in BOLD and CBV scans.

Methods

Experiments were performed on a vertical 4.7T Bruker BioSpec on four anesthetized monkeys (*macaca mulatta*, 6 experiments) weighing 4-8 kg, while the monkeys were viewing a rotating checkerboard (Fig. 1a) alternating with a gray screen (block design with 48s on-off periods, 64 images). The setup and methods have been described previously [3,4]. Anesthesia was a balanced remifentanyl/mivacurium regimen. Multi-shot GE-EPI functional images were acquired at a resolution of 0.5x0.375x2 mm^3. TE/TR was 20/750 ms. To measure CBV, 8 mg/kg MION was administered intravenously. Scanning parameters and stimulus paradigm were identical for BOLD and CBV-scans. CBF was also measured in several experiments using a single-shot triple-echo sequence [5]. Data were analyzed using custom routines in MatLab (the MathWorks).

Results

The visual stimulus has been shown to elicit a negative BOLD response in the primary visual cortex (V1) of monkeys and humans [1,2]. This is shown in Fig. 1b. The functional CBV response in the same slices is shown in Fig. 1c. While the BOLD response shows retinotopically matched activations and deactivations, the CBV increased in the stimulated and non-stimulated area, meaning that both positive and negative BOLD responses are accompanied by increases in CBV. Fig. 1d shows voxels that were significantly activated in both BOLD and CBV-scans, and indicates that the CBV increase in non-stimulated areas is generally lower than the CBV-increase in stimulated areas. Functional CBF activation followed a similar pattern as the BOLD response, i.e. CBF was increased in stimulated regions and decreased in regions where the BOLD was negative, in agreement with earlier studies [2].

Conclusion

We found that both positive and negative BOLD signals are accompanied by increases in CBV. The decrease in neural activity in unstimulated areas [1] leads to a negative BOLD response and decreased CBF, but increased the CBV. This could be due to an uncoupling of CBV and CBF in the inhibitory region, although it is also possible that the discrepancy between CBF and CBV has its origin in the fact that the different methods sample different vascular compartments.

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References: [1] Shmuel et al., Nat. Neurosci. 9: 569-577 (2006); [2] Shmuel et al., Neuron 36: 1195-1210 (2002); [3] Logothetis et al., Nat. Neurosci. 2: 555-562 (1999); [4] Goense et al., Magn. Reson. Imag. 28: 1183-1191 (2010); [5] Yang et al., Magn. Reson. Med. 52: 1407-1417 (2004)