Decreased cerebral blood volume and flow in areas with negative BOLD indicates the mechanism for negative BOLD may be stimulus- and area-specific

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Introduction

Using ring-stimuli, we showed increased cerebral blood volume (CBV) in regions with negative BOLD responses in monkey primary visual cortex (V1) [1]. This seemingly disagrees with earlier work in cat visual cortex, where CBV decreased in regions with negative BOLD [2]. However, the negative BOLD in cats occurred beyond the primary visual cortex, in the suprasylvian and ectosylvian gyri. In this study, we aim to reconcile these differences by investigating the mechanism for negative BOLD in peripheral V1 and extrastriate visual cortex in monkeys.

Methods

Experiments (N = 6) were performed on a vertical 4.7T Bruker BioSpec on 3 healthy anesthetized monkeys (*macaca mulatta,* two males, one female, weight 4-9 kg), while the monkeys were viewing rotating checkerboard stimuli alternating with a gray screen, or flickering LEDs. The methods have been described previously [1,3,4]. Anesthesia was a balanced remifentanil/mivacurium regimen. BOLD and CBV were measured using a multi-shot GE-EPI with TE/TR of 20/750 ms. For CBV-measurements, 8 mg/kg MION was administered intravenously. Cerebral blood flow (CBF) was measured using a single-shot FAIR with TI/TR of 1400/4500 and the shortest possible TE (8-10 ms). Data were analyzed using custom routines in MatLab (the MathWorks). All experiments were approved by the Regierungspräsidium BW (DE) and were in full compliance with the guidelines of the EU (EUVD 86/609/EEC).

Results

Figure 1 shows the BOLD- and CBV activation maps in a representative animal. Functional CBV (C-D) was decreased (positive) in areas where the BOLD response was negative; CBF was also decreased in these areas. The areas with negative BOLD corresponded to peripheral V1 (>15-20 degrees of visual angle) and extrastriate areas V2-V4. The CBF response showed a similar pattern as the BOLD response, with increases at the operculum and decreases in the periphery and extrastriate cortex. Flickering LEDs elicited positive BOLD throughout V1 and negative BOLD in areas V2-V5.

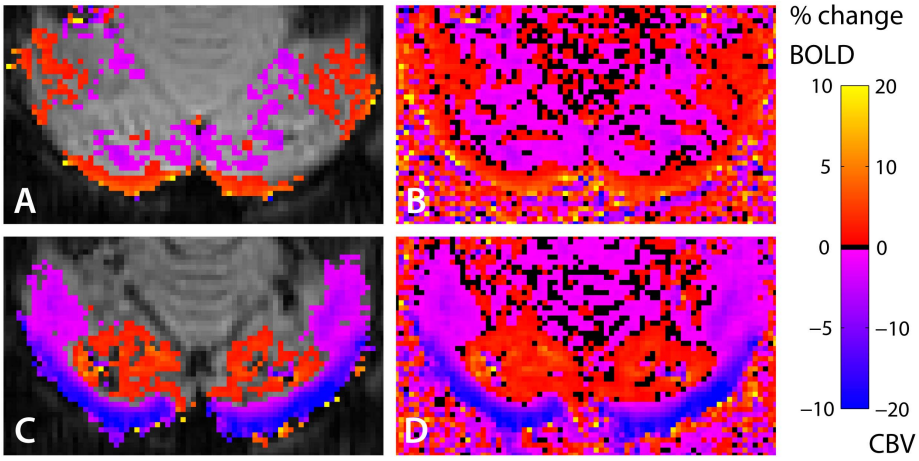

Figure 1
Functional activation in early visual cortex in response to a rotating checkerboard stimulus. The BOLD activation map (A) shows positive activation at the V1-operculum, accompanied by negative activation in peripheral V1 and extrastriate areas. B: raw BOLD-map. The functional CBV-map obtained using MION (C) shows a signal decrease at the V1-opercolum and a signal increase in peripheral V1 and extrastriate areas. D: raw MION-based CBV map.

Conclusion

We found that the mechanism for negative BOLD in peripheral V1 and extrastriate visual cortex upon full-field stimulation differs compared to the negative BOLD elicited with ring-stimuli [1]. The negative BOLD is accompanied by decreases in CBV and CBF and is probably similar to the negative BOLD observed in the suprasylvian and ectosylvian gyri in cats [2]. Our results suggest that more than one mechanism for negative BOLD exists, and the negative BOLD mechanism may be area-dependent.

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References: [1] Goense et al., Neuron 76: 629-639 (2012); [2] Harel et al., J. Cereb. Blood Flow Metab. 22: 908-917 (2002); [3] Logothetis et al., Nat. Neurosci. 2: 555-562 (1999); [4] Goense et al., Magn. Reson. Imag. 28: 1183-1191 (2010).