

Is the negative BOLD response a gain control mechanism?

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Introduction: In the visual system, the negative BOLD response (NBR) is a decrease in BOLD contrast in one part of the visual cortex in presence of a spatially-distant, modulated inducer. The NBR is believed to be caused primarily by an active process that reduces ongoing neural activity outside the region of positive BOLD response (PBR) rather than by passive 'vascular steal' (Shmuel, Yacoub et al. 2002; Shmuel, Augath et al. 2006). The NBR is linearly-related to the positive BOLD response in the inducing region but measurements of this relationship indicate a small but significant residual NBR as the PBR tends towards zero. In other words, the NBR at zero background contrast can be modeled as

$$N=aP+k \quad [1]$$

where N is the magnitude of the NBR, P is the magnitude of the PBR and a and k are variables. An NBR is possible even when the surround region has zero contrast because the activity of cortical neurons can be suppressed below their resting baseline.

However, at least two models of the NBR signal mechanism are consistent with these measurements. In the first model, ongoing neural activity in the suppressed region may simply be scaled by an incoming suppressive signal that has the form of [1]. This model would predict that

$$N=(aP+k)B \quad [2]$$

where B is a background neural activity in the suppressed region. N is therefore proportional to B and the NBR is a pure multiplicative gain change similar to that found for early contrast normalization processes.

Alternatively, the NBR may be caused by an absolute reduction in the ongoing neural activity. In this case, assuming an approximately linear relationship between neural activity and BOLD response (Boynton, Engel et al. 1996) the magnitude of the NBR is independent of the ongoing-neural activity in the suppressed region and is simply described by equation [1]. In this form, the effect of the NBR would appear similar to that measured recently for attentional modulation of the BOLD signal (Buracas and Boynton 2007).

General methods: All scans were performed on a Siemens 3T Tim Trio scanner at the UCSF Neuroscience Imaging Center. Subjects viewed stimuli presented on a calibrated LCD screen in a shielded box via a single front-surface mirror. T2*-weighted data were acquired using a stock Siemens EPI sequence and co-registered to high-resolution MPRAGE structural anatomies. Data were visualized and analyzed on flattened representations of the visual cortex using the Stanford VISTA toolbox. In addition to the NBR experiments described below, early visual areas were identified for each subject using standard fMRI retinotopic mapping techniques. We presented stimuli in both block-design and event-related paradigms in which we independently varied the contrast of the central inducing region and the eccentric surround. We measured BOLD responses from both regions in retinotopically-defined early visual areas and attempted to fit them to the two model of NBR described above. In the block-design experiments, we measured a true NBR: a reduction in the background BOLD response in the presence of an inducer. In the event-related experiments, the background response was always positive but its magnitude varied depending on the contrast of the central inducer region. In both experimental conditions, the subject's attention was strongly-controlled by a demanding foveal task and the effects we observe are not caused by attentional modulation.

Results: In both types of experiment, the NBR amplitudes were well-fit by a simple subtractive model with no dependence on ongoing surround activity. We conclude that the NBR is best-modeled as a pre-attentive subtractive effect (Equation [2]) although this may be due to a combination of multiplicative gain changes in a small subset of visual neurons and a less selective general reduction in activity across the entire population. The mechanisms that give rise to the NBR may operate in a manner similar to those responsible for attentional modulation.

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