Contrast and duration dependence of the negative BOLD response to visual stimulation in visual and auditory cortical regions at 7T

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Target audience: neuroscientists and clinicians interested in the study of the negative BOLD response.

Purpose: Negative BOLD responses to external stimulation are often found in various brain regions[1,2]. Growing evidence supports the association of negative BOLD with local neuronal deactivation, giving functional meaning to this phenomenon[3,4]. The aim of the present study was to characterize, in humans, positive (PBRs) and negative BOLD responses (NBRs) to visual checkerboard stimulation of varying contrast and duration, focusing on NBRs occurring in both visual and auditory cortical regions. The higher functional sensitivity available at 7T allowed obtaining more precise response estimates at fine spatial resolution (1.5mm), especially relevant for auditory NBRs.

Methods: 10 healthy subjects were scanned at 7T with multi-slice GE-EPI (TR/TE=2000/25ms, 1.5×1.5×1.5mm^3 spatial resolution). Subjects were presented with visual stimuli consisting of 8Hz flashing checkerboard stimulation periods, alternated with 20s fixation. Three paradigms were applied: a functional localizer (*FLoc*), comprising 8 blocks with 10s stimulation periods, using checkerboards at 20% contrast; a contrast-varying run (*FCont*), comprising 32 blocks with 10s stimulation with checkerboards presented at one of 4 different contrast levels: 2%, 5%, 20% or 80% (counter-balanced, 8 repetitions/level); a duration-varying run (*FDur*), comprising 32 blocks with stimulation periods of 4s, 10s, 16s or 20s (counter-balanced, 8 repetitions/duration), using 20%-contrast checkerboards. FMRI data were motion-corrected, brain-extracted and detrended. Physiological and motion confounds were identified with ICA and included in subsequent GLM analyses as regressors of no interest. Based on the *FLoc* run, 3 ROIs were defined: (a) occipital PBR regions, (b) occipital NBR regions, and (c) temporal lobe NBR regions (BA41-42). These ROIs were then co-registered to *FCont* and *FDur* image spaces, and responses were averaged within those regions, excluding voxels containing large draining veins.

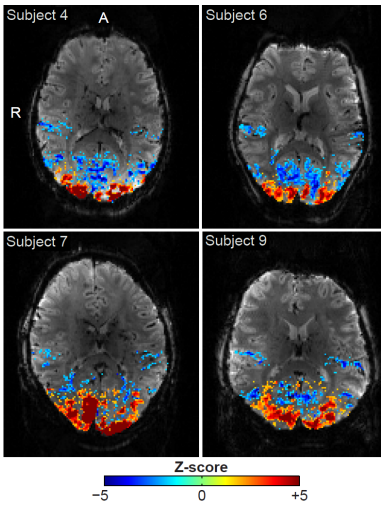

Fig 1. Examples of ROIs with significant positive and negative BOLD responses to visual stimuli, in *FLoc* data.

Results: Based on *FLoc* data, clusters with large positive Z-scores were found mainly in the visual cortex, while clusters with negative scores were found in the visual and in the primary auditory cortex (Fig.1). Across subjects, visual PBRs and both visual and auditory NBRs significantly depended on stimulus contrast ($p<0.01$) and duration ($p<0.05$) (Fig.2). Response amplitudes increased monotonically with contrast, with both visual and auditory NBR amplitudes linearly coupled to the visual PBR amplitude (Fig.2d). For stimuli with durations of 4–10s, the areas under the response curves increased with stimulus duration and all responses remained linearly coupled (Fig.2h). For longer stimulation periods, however, both NBRs exhibited earlier returns to baseline than the PBR (Fig.2f,g), resulting in a reduced normalized response relative to the PBR (Fig.2h).

Conclusion: Under the hypothesis of neuronal deactivation, these findings suggest a highly dynamic system of visual-auditory interactions, sensitive to stimulus contrast and duration, which can occur even for the passive observation of low attention-demanding visual stimuli. The uncoupling effects observed with longer stimuli suggest either that neuronal deactivation may be more quickly attenuated in time than neuronal activation, or that the neurovascular coupling properties of NBRs may differ from those of PBRs.

References: **(1)** Shmuel A, et al. Neuron 2002. **(2)** Laurienti P, et al. Journ. of Cogn. Neurosc. 2002. **(3)** Shmuel A, et al. Nat. Neurosci. 2006. **(4)** Mullinger KJ, et al. NeuroIm 2002.

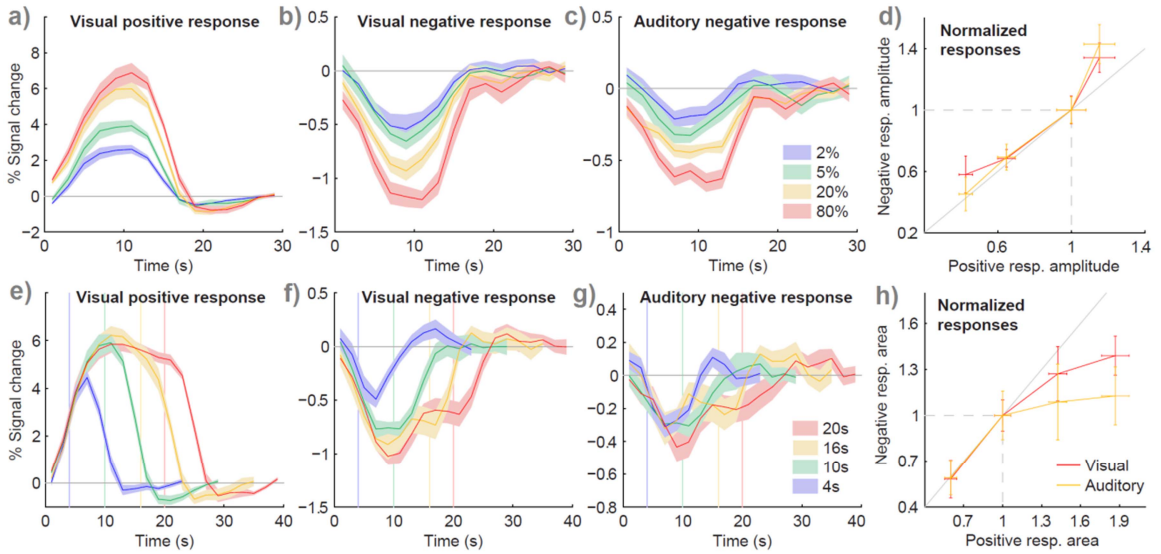

Fig 2. Group average BOLD responses to varying-contrast (a-d) and varying-duration (e-h) visual stimuli. Response curves and amplitudes represent averages across blocks and across subjects, with error margins representing the standard error across subjects.