Correlation of post-stimulus undershoot with BOLD response in event-related fMRI

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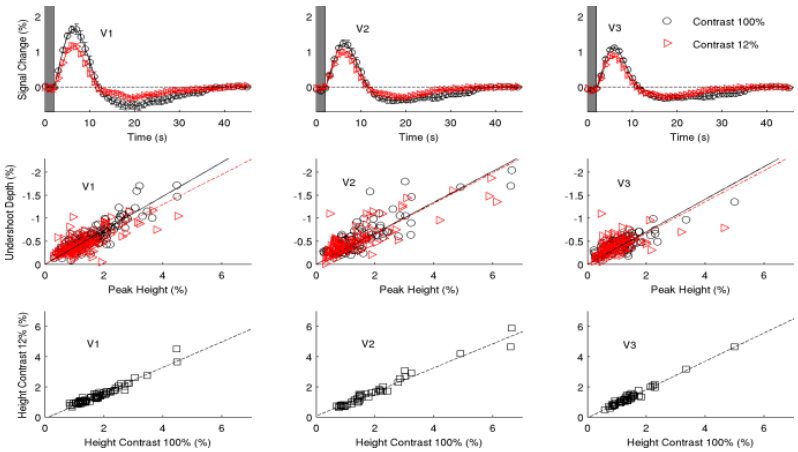
Introduction: Event-related (ER) BOLD-fMRI has been broadly used in brain activation studies for detecting the BOLD response to brief stimuli or events, and offers a means for quantitatively investigating the relationship between the elicited BOLD response and the corresponding neural events. For a single event, the dynamic BOLD response reflects the temporal evolution of the combined effects of the underlying physiological changes accompanying the neuronal activity; after a small initial dip, the response increases for a few seconds and then decreases to baseline, followed by a post-stimulus undershoot before returning to the baseline [1]. The initial dip, occurred during the first 2 s after stimulus onset and observed in some experiments, was attributed to an initial increase in deoxyhemoglobin that resulted from the increase in oxygen extraction prior to the elicited dominant blood flow and blood volume increases. The positive BOLD response reflected an overall decreased deoxyhemoglobin that resulted from the dominant increases in blood flow and blood volume. The origin of the post-stimulus undershoot remains an active research topic reflected in recent studies [2-4]. It is an open question whether there exists a quantitative relationship between the positive BOLD response and the negative post-stimulus undershoot. Understanding this relationship has important implications for the interpretation of ER-fMRI studies aiming to infer the neuronal activity from the hemodynamic parameters. In this study we investigate this relationship in visual areas V1, V2 and V3 using an ER paradigm with voxelwise analysis.

Methods and Materials: Six subjects participated in the study (ages from 20 to 59). Two subjects were scanned twice on two separate days. Functional brain images of 16 slices covering the whole occipital cortex were acquired with a gradient echo EPI sequence (TR = 1 s). The in-plane resolution of the images is 3.59×3.59 mm^2 and the slice thickness is 4 mm. Subjects were presented two visual stimuli consisting of a polar checkerboard pattern (diameter 18.1 degree) with two different Michelson contrasts: 12% and 100%. For each trial, one stimulus was presented for 2 s and contrast reversed at a rate of 10 Hz, followed by 44 s of blank screen with the mean luminance of the stimuli. Each scan had 4 trials for each stimulus presented in a pseudo-random order, and each subject had 5 scans. In addition, each subject also had a standard retinotopic mapping protocol for delineating visual areas. The subjects were instructed to fixate at a mark displayed at the center of the visual field and to respond to the mark's color changes with hand button press for attention control during all functional scans. *Image processing and data analysis:* After preprocessing of the functional images with AFNI [5], the voxel-by-voxel signal intensity time course for each scan was normalized by its mean. These signal change time courses from all scans were further sorted according to the stimulus contrast and then combined together to form one signal change time course including all trials for each contrast. For each contrast, the cross-correlation coefficient (ccc) between the sorted signal change time course and an ideal hemodynamic response function was computed. Activated voxels were determined as those with ccc>0.11 (p =0.0008) for both contrasts. For each activated voxel, a mean signal change time course was obtained by averaging the signal change time courses across all the trials of the same contrast. The peak height of the mean signal change time course was computed as the mean of the three neighboring data points around the peak, and the undershoot depth was computed as the mean of the five neighboring data points around the bottom. All activated voxels within each visual area were included to form a region of interest (ROI) for that area, and a ROI averaged signal change time course was further computed by averaging the mean signal change time courses over all the voxels within the ROI.

Results and Discussion: The upper panel in the figure shows the group-averaged (n=8) ROI mean signal change time course in V1, V2, and V3, respectively. The gray vertical bar represents the visual stimulation. Post-stimulus undershoots are present in all visual areas; they started at about 12 s after stimulus onset and returned to baseline at about 35 s. The larger the response, the deeper the undershoot, suggesting a correlation between the two. A voxelwise analysis showed a significant correlation between the positive response and the negative undershoot for the activated voxels in each visual area for each subject (the maximal p<0.05). The middle panel shows a scatter plot of undershoot depth versus peak height for the activated voxels in V1, V2, and V3, respectively, for a representative subject. The black solid and red dashed lines are least-square-fits to the scatter plots for the 100% and 12% contrasts, respectively. The group-averaged correlation coefficients are 0.73±0.17 (mean±SD), 0.71±0.17, and 0.71±0.20 at 100% contrast and 0.58±0.17, 0.53±0.17, and 0.57±0.20 at 12% contrasts in V1, V2, and V3, respectively. Across the visual areas the significant correlation of undershoot depth with peak height demonstrated a highly homogeneous hemodynamic response to the brief visual stimulation, though the response magnitude varied substantially within each of the visual areas. The lower panel shows a strong correlation of peak height between the 12% and 100% contrasts in V1, V2, and V3, respectively, for the representative subject (the maximal p<2.9×10^{-7}). The group averaged correlation coefficients are 0.94±0.07, 0.92±0.10, and 0.93±0.07 in V1, V2, and V3, respectively. These results further support that the elicited hemodynamic response is highly homogeneous across the visual areas. In conclusion, the dynamic BOLD response to a brief visual stimulation is highly homogeneous across the visual areas and the negative undershoot is correlated with the positive BOLD response, suggesting a common impulse hemodynamic response across the visual areas.



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Reference: 1. RB Buxton, et al., 1998. MRM 39:855-64. 2. J Frahm, et al., 2008. NeuroImage 40:473-81. 3. MJ Donahue, et al., 2009. J Cereb Blood Flow Metab 29:1856–66. 4. JJ Chen & GB Pike, 2009. NeuroImage 46:559-68. 5. RW Cox, 1996. Comp Biomed Research 29:162-173.