Laminar Analysis of the BOLD Hemodynamic Impulse Response

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Introduction

The character of the BOLD hemodynamic impulse-response function (HIRF) is of strong interest in neuroimaging because it determines the spatial and temporal accuracy of fMRI measurements. We used high-resolution MR methods to examine the time course of the HIRF as a function of depth within early visual cortex. These measurements could help to explain the vascular mechanisms of the BOLD response.

Methods

MR imaging: Functional images were obtained on a 3T scanner using BOLD contrast, a spiral readout and pixels varying from 0.8—1 mm, 10-cm FOV, 8 1-mm slices, TE = 25 ms, TR = 750 ms, 2 interleaves, and a custom 6-cm-diam receive-only surface coil. Nearly coronal slices were chosen to cover the most caudal portion of the occipital lobe (early visual cortex). High-resolution (0.6-mm-isotropic) T1-weighted anatomical images were obtained on the same slice prescription to facilitate subsequent registration. Protocol: Subjects (N=3) viewed 4-Hz flickering "checkerboard" patterns presented on a flat-panel display. To control subject attention, they spent the majority of their time performing a contrast-discrimination task upon a small annulus (0.5—1.25º visual eccentricity). Once every 27—30 s, a high-contrast outer annulus (1.5—2.5º) was briefly presented (0.75 s) following a visual cue. Thus, we created short (<2 s) periods of activity in the gray-matter corresponding to the outer annulus. Subjects performed this task for 8—12 3-min runs. Data analysis: Each run was corrected for motion and to remove slow trends. The HIRF was then estimated by finding the mean and SEM for each time point across the many (typically 72) events. This data was then aligned to a high-resolution (0.6-mm isovoxels) T1-weighted anatomical reference volume that had been segmented to identify the gray-white boundary. A distance map from this boundary provided a depth coordinate, *s*. Laminarly resolved HIRFs were obtained by averaging voxel time series in a range of depth within retinotopically defined subregions of areas V1, V2, and V3. These subregions were additionally restricted to gyral and sulcal regions because of their stereotypical differences in gray matter thickness.

Results

The positive-going BOLD HIRF is dominant within the gray matter. Some signal is observed in the white matter and CSF immediately adjacent to the gray matter, but this could be caused by partial-volume effects. In a gyral subregion of area V1 (Fig. 1), the amplitude of the signal peaks toward the pial edge of gray matter. In gray matter, all HIRFs show the usual initial positive lobe, followed by a strong undershoot and slow return to baseline. The character of the HIRF changes through the depth of gray matter. In particular, the initial onset of the positive lobe becomes more-and-more delayed as *s* increases outward from the white matter. These changes are accompanied by a lengthening period of increasingly negative-going signal during the early portion of the response. The negative-going lobe is particularly pronounced for $s = 3.5$ mm. This is nominally just outside the pial surface, but alignment errors are possible. Much the same pattern is evident in a gyral subregion of area V2D (Fig. 2), except that the response amplitude reaches its peak value more deeply within the gray matter, at $s \sim 0.75$ mm. A similar laminar pattern of activity was observed in a second subject.

Discussion

The BOLD HIRF shows significant variations within the depth of the early visual-area cortex. An initial period of negative-going signal is evident in the most superficial gray matter, and is even more apparent just outside the brain; this could be the "initial dip." The presence of the initial dip just outside the brain and only in the most superficial layers of cortex suggests a laminar distribution of vascular control points[1]. The more superficial vasculature could be upstream of the control points, so that activation creates a small pressure drop in these vessels, producing a negative dip. By permitting the observation of such structure/function relationships, these laminar measurements of hemodynamics should help to elucidate the detailed vascular mechanisms of the BOLD response.

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[1]Harrison, RV et al., Cereb Cortex **12**, 225 (2002).

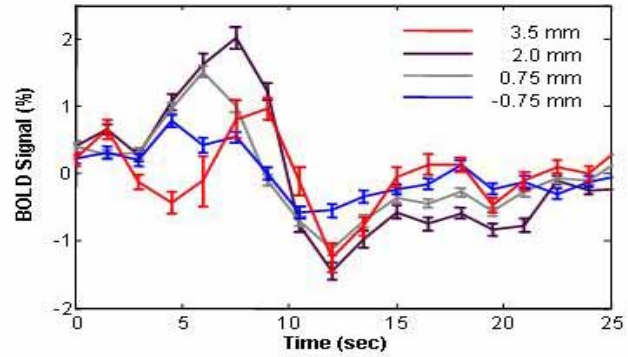

Figure 1: BOLD HIRFs versus laminar depth for area V1.

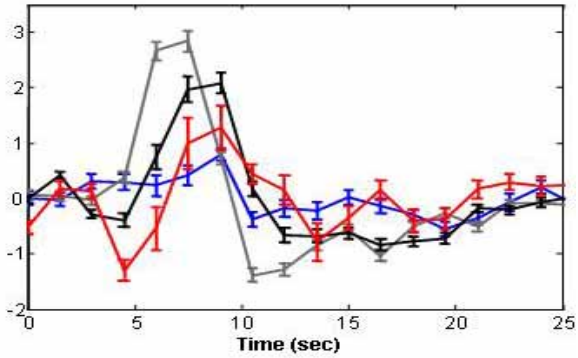

Figure 1: BOLD HIRFs versus laminar depth for area V2.