Comparison of Diffusion and Hemodynamic Response Functions in Human Visual Cortex

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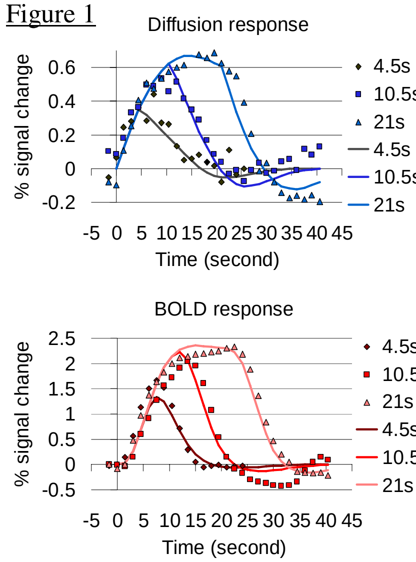
Using heavily diffusion-sensitized MRI, a transient signal increase in the occipital cortices in response to visual stimulation has been observed[1]. The most striking finding was that the onset of the response in the diffusion-weighted fMRI (DfMRI) signal was always earlier than that of BOLD signal by 2-3s. In the present study, we investigated the temporal characteristics of the DfMRI signal under the assumption of a linear, time-invariant system[2] and estimated an intrinsic diffusion response function (DRF), as a counterpart to the hemodynamic response function (HRF) in BOLD-based fMRI.

Figure 1



MATERIALS AND METHODS

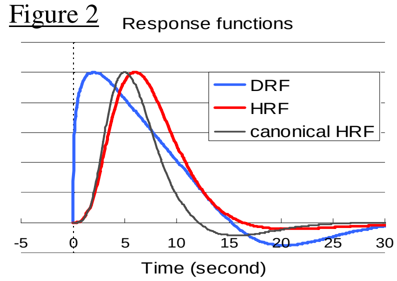
Subjects: To define the DRF, we conducted 18 experimental sessions on 14 healthy subjects. Every subject participated in only one session except for 3 subjects that contributed in more than one condition. We discarded 4 sessions because of either head motion or poor/unstable activation in the BOLD fMRI runs. Validation of the DRF was done on another 2 subjects.

Data acquisition: We used a 3T MRI scanner equipped with an 8-channel phased-array coil. Diffusion-weighted images were acquired using a twice-refocused spin echo sequence. Acquisition parameters were: 96x96x10 matrix, voxel size=2x2x3mm^3, TE=89ms/TR=1.5s. Motion-probing gradient was given in only one direction [1,1,1] with a b-value of 1800s/mm^2. A simple visual stimulation using an 8Hz-flickering dartboard was given for one of 3 durations (4.5s, 10.5s, 21s) fixed for each experimental session. A 3D T1-weighted image was acquired to define the volume of interest (VOI) in the early visual cortices.

Data processing: We used SPM5 software package for preprocessing including slice-timing correction and realignment[3]. Raw signal time courses were obtained by pooling the signal from each stimulus duration over individual VOIs manually defined to include *all* the gray matter voxels in the early visual areas. The time courses were then used to estimate the DRF and the HRF from the DfMRI and BOLD data, respectively, by least squares fitting with a pair of gamma density functions (f_1 for the positive response, f_2 for the negative undershoot):

$$f_i(x)=\frac{\lambda_i^{\alpha_i}}{\Gamma(\alpha_i)}x^{\alpha_i-1}e^{-\lambda_i x}\ ,\ i=1,2\ ,\ x>0$$

Figure 2

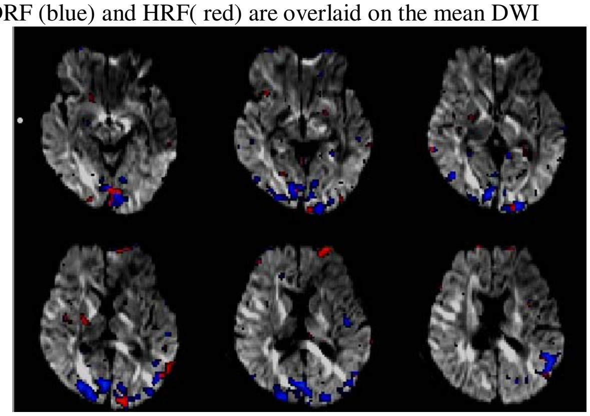


RESULTS

Figure 1 shows the diffusion (top) and the BOLD (bottom) responses to the 3 stimulus durations with the curves showing the modeled responses. The monotonous increase of response amplitude indicates that the assumption of linear time-invariant system holds in DfMRI. The time-to-peaks of the empirical response functions clearly reflect the steepness of the actual responses (Figure 2 and Table 1, including the canonical HRF for comparison). In addition to the steeper onset, the DRF is also wider than the HRF to account for the cumulative increase in the response amplitude. Figure 3 shows a SPM from one of the validation datasets with non-synchronized onsets (i.e. jittered to the TR) and randomized inter-stimulus intervals. The DRF had a higher sensitivity in the majority of those "activated" voxels detected using either DRF or HRF (p<.01, uncorrected).

Table 1	Time to peak	α_1	λ_1	α_2	λ_2	Ratio f_1/f_2
DRF	1	8	7	22	2	3.5
Canonical HRF	5	6	1	16	1	6
HRF	6	7.5	1.5	20	2.5	8

Figure 3. Validation of the DRF. Activated voxels better fit with DRF (blue) and HRF(red) are overlaid on the mean DWI



DISCUSSION

The response functions estimated from the signals in the early visual cortices clearly show that the diffusion response is faster and more asymmetric than the BOLD response. The DRF is characterized by a steeper onset and a slow return to baseline, with a striking resemblance with optical signal detecting a local extracellular volume change during neural activity[4], suggesting the DfMRI signal is related to some geometric changes in brain tissue upon activation.

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