Characterization of the BOLD Hemodynamic Response Function at 7T: towards separation of vasculature and parenchyma

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Introduction

A limitation of T_2^*weighted BOLD fMRI is the confounding contribution of signal from the larger vasculature. An improved BOLD specificity to parenchyma can be achieved at high field strengths such as 7T due to increased contrast-to-noise ratio, and reduced contribution of intravascular signal as compared to lower field strengths. Moreover, at 7T high spatial and temporal resolution of the BOLD signal can be achieved [1], making it possible to investigate the BOLD response in much finer detail. Previous human work at 3T has shown that the temporal characteristics of the BOLD response in the visual cortex are related to the organization of the local vasculature [2]. A correlation of the time-to-peak (TTP) and width (FWHM) of the BOLD response function was shown. Based on this previous work we expect to obtain a better separation between parenchyma and the macrovasculature at a high resolution. We characterized the spatio-temporal properties of the BOLD response in the visual cortex at 7T using an event-related fMRI paradigm with very short visual stimuli, higher sampling rate, and for different spatial resolutions.

Materials and Methods

Data acquisition: Five healthy volunteers were scanned on a Philips 7T system with a 16 channel SENSE head coil. Functional data was obtained using a multislice single-shot GE-EPI acquisition with TR/TE=440/27ms, FA=60°, SENSEfactor=2.2, four different isotropic voxel sizes with dimensions: 1, 1.5, 2 and 2.5mm with slice gap 1.5mm, 1mm, 0.5mm and 0mm respectively; FOV=150×120 mm^2, and 7 coronal slices (3 slices for the 1mm scan) covering visual areas V1 and V2. The bandwidth in the phase-encode direction was set to 2300Hz for all voxel sizes, to ensure the same geometric distortions. 3rd order image based shimming on the FOV of the functional scans after brain extraction using BET [3]. A whole brain 0.6mm isotropic T_2^*w scan was acquired as an anatomical reference. Cardiac and respiratory rate data were recorded during all scans. *Functional Paradigm:* Each functional scan consisted of four parts; i) 31s baseline period, ii) 437s event-related (ER) part, iii) 31s baseline period and, iv) 79s block design (localizer) part with off/on periods=15.8/15.8s (uniform gray screen / 8Hz reversing checkerboard). The event train for the ER part was generated with interstimulus intervals (ISI) taken from a uniform permuted distribution between 6*TR=2.64s and 26*TR=11.44s in 1*TR steps [4]. A total of 61 stimuli were presented with stimulus duration of 250ms (two 125 ms opposing checkerboard frames) and a mean ISI of 7.04s. All conditions included a central red fixation point. *Data processing:* The functional scans were 2D realigned, corrected for cardiac and respiratory fluctuations and linear trend [5, 6]. The localizer part was processed using FEAT: high pass filtering (cut-off at 1/31.6 Hz.), slice timing correction, and no spatial smoothing [7]. The largest significant cluster (cluster P threshold = 0.05, Z threshold=3.5) was selected and used as a region of interest for the ER-fMRI analysis for the corresponding voxel size. A vein region mask was created on the 1.5^3 mm^3 scan using the temporal noise-to-signal-ratio (tNSR) of the baseline periods, where high tNSR spots depict veins, and the high resolution T2*-weighted scan, where low signal intensity spots reveal veins. Voxels adjacent to these veins were also included in the mask. Also, a manually delineated mask containing approximately visual area V1 was created on the 1.5^3 mm^3 scan using the high resolution T2*-weighted scan as anatomical reference. Estimation of the hemodynamic response function (HRF) was done by means of conjugate gradients for deconvolution [8] after normalization by the baseline (mean of the two baseline periods), 4-fold Fourier interpolation and temporal smoothing (loess with span 0.15 [9]). Active voxels were separated in a vein compartment as depicted by the vein region mask, and a remaining compartment (referred to as the 'non-vein compartment). Next, for every HRF in the vein and non-vein compartment we computed the time-to-peak (TTP), after slice timing correction, full-width at half maximum (FWHM) and maximum percent signal change (MPC). A further separation of the voxels in the non-vein compartment was done on the basis of different TTP; fast (2s–meanTTP) and slow (meanTTP–6s).

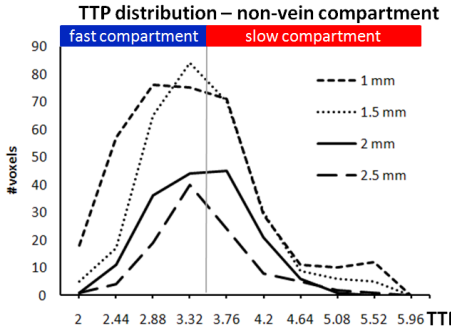

Figure 1

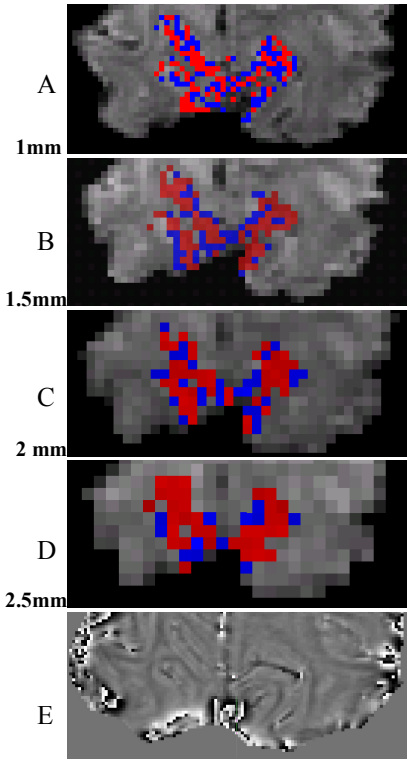

Figure 2

Results

The average correlation between TTP and FWHM across subjects and voxelsizes for all active voxels (vein and non-vein compartment) was 0.43±0.16, in agreement with previous results [2]. Overall the TTP, FWHM and MPC values were higher for the vein compartment. The TTP and FWHM distributions became broader with decreasing voxel size. The TTP distributions for the non-vein compartment for all voxel sizes are shown in figure 1 for a representative subject. Figure 2 A-D illustrates the increased TTP spatial heterogeneity with decreasing voxelsize. At the smallest voxelsize the slow responses (in blue) were predominately localized along the sulci, while the fast responses (in red) were predominately localized in neighbouring parenchyma. This correspondence to the underlying anatomy was reduced with increasing voxelsize (see phase image of T_2^*w for underlying anatomy in figure 2-E).
For the smallest voxelsize the average BOLD responses are shown for all compartments in figure 3. These findings were similar for all subjects.

Discussion

For the 'non-vein' compartment it is apparent that the increasing width of the TTP distribution with decreasing voxelsize reflects more TTP heterogeneity when scanning at a higher resolution. It is seen that at 7T, using short stimuli, small isotropic voxels and high sampling rate, a temporal resolution of the BOLD response can be measured which allows for better separation of vasculature and parenchyma. This opens the possibility to probe layer specific TTP as shown previously in rats [10].

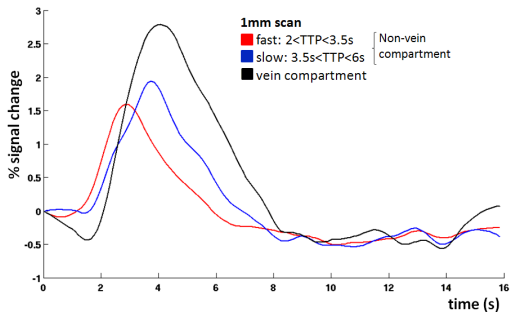

Figure 3

References

[1] Pfeuffer J et al NI (17) 2002, [2] Zwart JA. et al. NI(24) 2005, [3] Smith SM. HBM (17) 2002, [4] Hagberg GE. et al. NI (14) 2001, [5] Cox RW. CBR (29)1996, [6] Glover GH et al. MRM (44) 2000, [7] Smith SM. NI (23) 2004, [8] Ari N. et al IEEE/EMBS proc. 2001, [9] Cleveland WS. JASA (74);1979,[10] Silva AC. PNAS (12) 2002