Cortical depth dependent temporal dynamics of the BOLD response in the human brain

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Introduction: The spatial and temporal extent of the BOLD response is dispersed in relation to active neuronal sites due to the vascular organization and dynamics. The BOLD signal reflects an aggregate change from the microvasculature (diameters < 20 μm) directly serving the active sites, and the macrovasculature (diameters > 100 μm) that drains blood from several active sites [11]. The separation of the micro- and macro-vascular signals is not only essential in improving the specificity of BOLD fMRI but also to understand the mechanisms underlying neurovascular control. Recent animal studies at high field (≥7T) have shown that BOLD can be specific to the laminar vascular architecture of the cortex, by differences in its temporal dynamics in reference to cortical depth [1,2]. In the present work, we characterize the temporal dynamics of the BOLD response across cortical depth in the human primary motor (M1) and visual cortex (V1), at 7T.

Materials and Methods

Seven healthy subjects were scanned on a Philips 7T system with a 16 channel SENSE head coil. *Visual cortex (5 subjects):* Functional data were obtained using a multislice single-shot GE-EPI acquisition with TR/TE=440/27ms, FA=60°, SENSE factor=2.2, isotropic voxelsize of 1.5 mm^3, 1mm slice gap; FOV=150×120 mm^2, and 7 coronal slices covering visual areas V1 and V2, and 3rd order image based shimming [3]. A whole brain 0.6mm isotropic T_2^*w scan was acquired as an anatomical reference. *Motor cortex (2 subjects)*: same as above except 13 oblique axial-sagittal slices covering the primary motor cortex were acquired (no slice gap), with a TR=880ms and FA=65°. Hand movements were recorded from both subjects using a DataGlove 5 Ultra MRI (5DT, Irvine, California USA, sampling rate 20ms) Cardiac and respiratory rate data were recorded during all scans. **Functional Paradigm***: Visual Cortex:* 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). 61 stimuli were presented in the ER part (mean ISI:7.04s) with stimulus duration of 250ms (two 125 ms opposing checkerboard frames). All conditions included a central red fixation point. *Motor cortex*: The same paradigm structure was used except the ER was 463 s long (mean ISI: 7.77s). 54 stimuli were presented as a color changing dot from red to green prompting a short fist clench action. **Processing***:* fMRI data were corrected for motion, physiological noise and linear trend [4, 5]. The localizer part was processed using FEAT: high pass filtering (cut-off at 1/31.6 Hz.), slice timing correction, and no spatial smoothing [6]. The largest significant cluster (cluster P threshold = 0.05, corrected) was selected and used as a region of interest for the ER-fMRI analysis. Large veins (and extravascular space) were identified based on their low intensity on high resolution T2*-weighted scan. Estimation of the hemodynamic response function (HDR) was done by means of conjugate gradients for deconvolution [7] after normalization by the baseline (mean of the two baseline periods), 7-fold Fourier interpolation (10-fold for the motor cortex data) and temporal smoothing (loess span 0.15 [8]). The time-to-peak (TTP), after slice timing correction, full-width at half maximum (FWHM) and percent signal change (PSC) was computed for voxels in V1 and M1. The dependency of TTP, FWHM, and PSC as a function of distance to the cortical surface was estimated where the cortical surface was delineated manually on the high resolution T2*w image after coregistration to the functional data (Fig1A). Next, the distance was divided in three sections; 0 – 1 mm, 1 – 2 mm and 2 – 3 and the average HDR and TTP, FWHM, PSC was computed for every section.

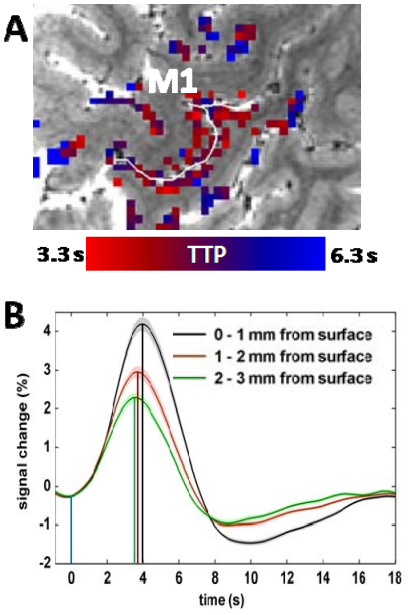

Figure 1

Results

Fig 1A and B show the spatiotemporal pattern in the TTP (motor cortex data) and the HDRs estimated for each cortical section respectively. Faster HDRs were also narrower and they appeared confined to the deeper gray matter (n=7). The delay in TTP was correlated with the FWHM of the HDR ($p < 0.01$). TTP, FWHM, and PSC decreased significantly with cortical depth (Fig. 2, where * for $p < 0.01$, † for $p < 0.05$ and ‡ for $p < 0.09$). The decrease in TTP with cortical depth was 0.22 ± 0.08 s/mm (V1) and 0.24 ± 0.07 s/mm (M1), computed from the linear fit slopes (mean ± std across subjects).

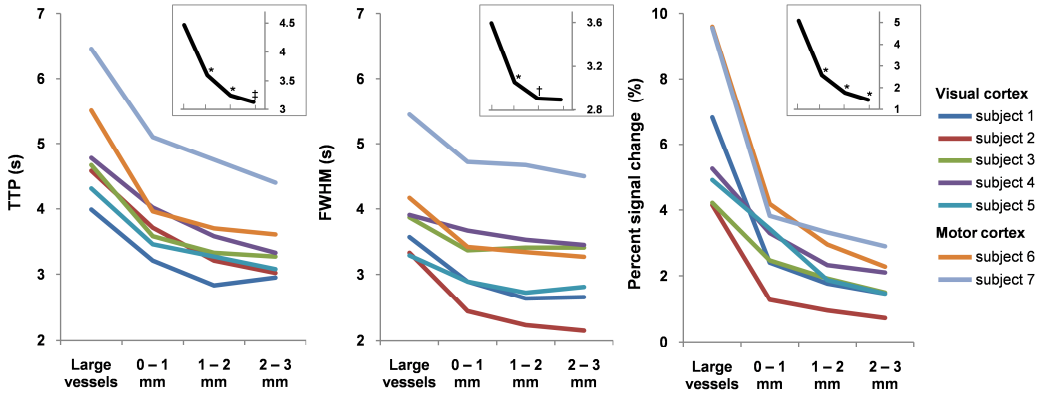

Figure 2

Discussion

Our results show that the shape and temporal dynamics of the BOLD response varies across cortical depth in the human brain, with faster and narrower responses corresponding to the deeper gray matter, and these measures increased in an orderly manner toward the cortical surface. Taking the average slope of TTP across grey matter depth and assuming a cortical thickness of ~3 mm, we estimate a pooling time of oxygenated blood contributing to the BOLD response from the deeper cortex to the pial surface of ~0.6 s (V1) and ~0.75s (M1), in agreement with a transit time of blood across the cortical vasculature of ~1s recorded in rat brain [9]. The FWHM of the HDRs in the deeper gray matter was on the order of 2.1 – 3.4 s (V1), and 3.3 – 4.5 s (M1), indicating a faster temporal resolution for the neurovascular coupling mechanism than previously reported in the human brain, and in line with reports in the rat brain [10]. The spatiotemporal heterogeneity of the BOLD response matches the known vascular organization across cortical depth [11], which is expected to be closely related to functional organization in the human cerebral cortex [12]. This opens the possibility to probe layer specific hemodynamics and neurovascular coupling mechanisms in human gray matter.

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