

Microvascular GE BOLD specificity and dynamics revealed by ultra high field MRI in humans

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Introduction

Gradient-echo BOLD is the most sensitive fMRI technique. Especially at high fields, it has opened up the possibility to visualize the columnar and laminar functional organization in the cortex [1-4]. However, the specificity of GE-BOLD can suffer from contributions of several vessel sizes even at high fields. Ideally, GE-BOLD should be specific to the microvasculature that directly perfuses active neuronal sites. Comparing the temporal evolution of the GE BOLD response with a microvascular response (spin-echo (SE) BOLD at high field [7]) can provide evidence on the specificity of GE BOLD fMRI. Recently we have shown that it is possible to obtain the microvascular hemodynamic impulse response function (HRF) using SE BOLD in combination with a dedicated surface coil at 7T [5]. Here we compare the SE and the cortical depth resolved GE HRFs using high spatiotemporal resolution and very short visual stimuli (250 ms). We show that the earlier part of the GE HRF (onset times and rising slope) in deep gray matter is very specific to the microvasculature shown by the close match with the SE HRF.

Materials and Methods

Data acquisition: Eight subjects were scanned on a Philips 7T system with a 16-channel surface coil [6]. GE/SE functional data (multislice single-shot EPI) was acquired with the following scan parameters: TR = 880ms, TE = 27/55ms, FA = 70°/125°, SENSE factor = 2/3, isotropic voxel size = 1/2mm³, EPI readout length = 34/27 ms, and 7/5 coronal slices covering V1. Local shimming (3rd order) was performed on the FOV of the functional scans [4]. A 3D T₂*w scan with 0.5mm³ isotropic voxel size was acquired as an anatomical reference. Cardiac and respiratory data were recorded during all scans. **Functional Paradigm:** The functional scan (10min) for both GE and SE consisted of four parts; i) baseline period, ii) event-related (ER) part, iii) baseline period and, iv) block design (localizer) part. The event train for the ER part was generated with interstimulus intervals (ISI) from an exponential distribution ranging between 2.9 – 19.6s [8]. Stimuli (N=54) were presented for a stimulus duration of 250ms (8Hz checkerboard). Stimulus onset was uniformly jittered relative to the TR, yielding a sub-TR temporal resolution of 220ms. **Data processing:** The functional scans were pre-processed identical to Siero et al. [4]. The largest significant cluster in V1 (cluster P threshold = 0.05, corrected) was selected and used as ROI for the ER-fMRI analysis. Large draining veins (and extravascular space) were excluded from the GE data using the T₂*w anatomical reference. Estimation of the HRF was done using deconvolution [9] after normalization by the baseline (mean of the two baseline periods), and 8-fold Fourier interpolation. For the GE data, the distance to the cortical surface was estimated for each HRF. The cortical surface was delineated manually in 3D on the T₂*w anatomy after coregistration to the GE data (Fig1, white contour) [4]. The GE HRF data was analyzed in three cortical depth sections; 0 – 1, 1 – 2 and 2 – 3 mm (Fig1: black, red and green lines respectively). The HRF onset time was defined by fitting a line to the slope between 20% and 80% of the peak of the HRF and computing the intercept with the baseline [11].

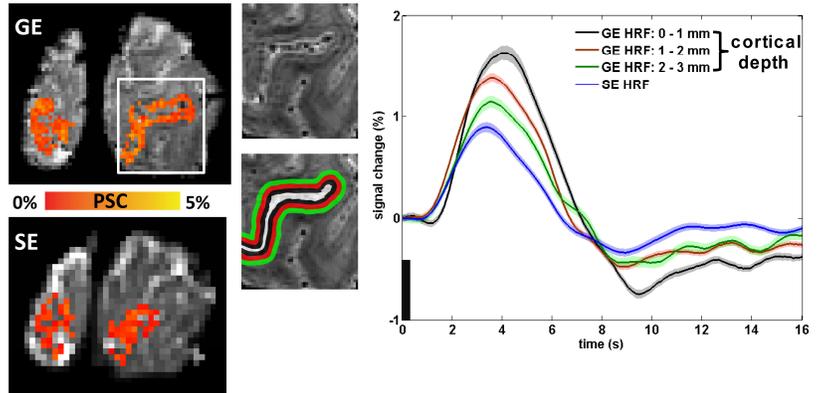


Figure 1: GE and SE data with percent signal change maps (PSC), T₂*w anatomy with cortical depth delineation, SE and GE HRFs across cortical depth. Black bar shows the stimulus onset and duration. Shaded areas indicate the standard error of the mean (SEM).

Results

Fig1 shows the GE and SE data with overlaid percent signal change maps, T₂*w anatomy with the cortical surface delineation (white contour) plus cortical depth sections, and the SE and GE HRFs across the cortical depth for a representative subject. Fig2 shows for all subjects the SE and GE HRF parameters: A) onset time, B) time-to-peak (TTP), C) full-width-at-half-maximum (FWHM), and D) percent signal change (PSC). Fig3 shows the direct comparison of the temporal evolution between SE and GE HRF in deep gray matter (1-2 and 2-3 mm) by looking at the ratio $\Delta R_2^*/\Delta R_2$ over time. The ΔR_2^* and ΔR_2 were computed by dividing the GE and SE HRF ($\Delta S/S$) by the used echo times [10].

Discussion

Our results reveal for the first time in humans the microvascular contributions of the conventional GE BOLD response across the cortical depth using very short stimuli and high spatiotemporal resolution. This is important as the microvasculature is most proximal to the neural active tissue and its dynamics are directly governed by the neurovascular coupling mechanisms. We find that the onset times and rising slope of the deep gray matter GE HRF closely matches those of the microvascular specific SE HRF (Fig2A, Fig 3). The increased TTP and FWHM of the GE HRF for all cortical depths, however, are potentially caused by non-specific blood flow and/or pooling in postcapillary venules and intracortical veins (Fig2 B, C). This is also seen by the increase of the ratio $\Delta R_2^*/\Delta R_2$ in the later part of the HRF (Fig3). By comparing the SE and the cortical depth resolved GE and SE HRFs we show that the early phase of the GE HRF is specific to the microvasculature in deep gray matter which presumably contains layers III-V.

References:

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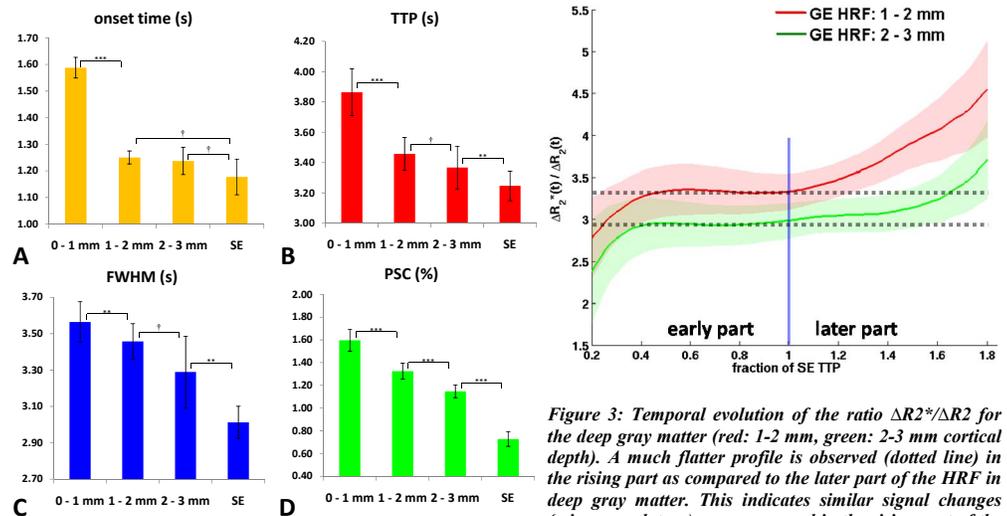


Figure 2: For all subjects, SE and GE HRF parameters across the cortical depth A) onset time, B) TTP, C) FWHM, and D) PSC. **** $P < 0.005$, ** for $P < 0.05$, † non significant $P > 0.1$).

Figure 3: Temporal evolution of the ratio $\Delta R_2^*/\Delta R_2$ for the deep gray matter (red: 1-2 mm, green: 2-3 mm cortical depth). A much flatter profile is observed (dotted line) in the rising part as compared to the later part of the HRF in deep gray matter. This indicates similar signal changes (microvasculature) were measured in the rising part of the GE and SE HRF. In the later part of the GE HRF additional signal changes are observable; an indication for non-microvascular contributions. Shaded areas indicate the SEM for all subjects.