Functional Quantitative Susceptibility Mapping (fQSM)

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Introduction

Functional activation maps based on BOLD-fMRI provide qualitative topologies of task-related modulus intensity changes which depend on physiological (magnetic susceptibility) and imaging (e.g. TE) parameters. As an attempt to relate BOLD changes to an absolute quantity and to render the comparison of BOLD-fMRI studies more reliable at the same field strength, fast T2*-mapping can serve as an alternative to T2*-weighted imaging. However, T2* is an MR-specific parameter and is field dependent. Its measurement requires the acquisition of two echoes per repetition, is sensitive to unwanted dynamic effects and to static, but non-local susceptibility gradient effects. Quantitative susceptibility mapping (QSM) uses phase information from MR images to calculate local tissue susceptibility. It has experienced significant development in recent years, partly due to the emergence of advanced background field removal methods [1-3]. This study introduces time-resolved functional QSM (fQSM) as a quantitative approach for BOLD-fMRI, and proposes a multi-step filtering algorithm for the calculation of maps showing activation induced susceptibility-changes.

Materials and Methods

Two volunteers were scanned on a 7T Philips scanner during a multi-task fMRI experiment. *Paradigm:* A visual, motor or somatosensory block-paradigm was presented, which alternated 12s blocks of task/stimulation with 18s blocks of rest; visual stimulus: a flickering checkerboard ring on a grey background, motor task: finger-tapping with the left hand, somatosensory stimulus: 60 Hz vibrotactile stimulation applied to the fingertips of the left hand. *Protocol*: Zoomed multi-slice GE-EPI data (TE=25ms, TR=3s) with 1mm isotropic resolution [4] spanning either the visual or the sensorimotor cortex. *Analysis:* Processing steps were performed in the following order for optimal temporal stability and statistical power. (i) Phase maps were masked using binarised modulus images. (ii) Global intensity variations along the slice direction were corrected by rewinding the phase in k-space [5]. (iii) Global temporal phase variations were corrected by using the phase at the origin of the k-space data as a nuisance regressor [6]. (iv) Spatial unwrapping was performed using a fast 3D algorithm [7], and was followed by temporal unwrapping. (v) The modulus data were motion-corrected using 3dAllineate (AFNI), and the resulting correction matrices were then applied to the phase data. (vi) High-pass spatial filtering was then performed with one of the following methods: homodyne Gaussian with kernel size 12mm, relative phase filtering by complex division with the first volume in the time-series [8], 8th order polynomial background field removal, SHARP with a threshold of 0.1 and a kernel size of 2mm [3] or dipole-fit with maximum number of iterations set to 100 [1,2]. (vii) The resulting phase-images, except for the relative phase filtered data-sets, were then divided by $\gamma B_0 TE \times 10^{-6}$ to yield field maps in ppm. (viii) These maps served as inputs directly for the calculation of phase-SPMs or for the QSM calculations. Susceptibility maps (QSM) were calculated by using an iterative deconvolution algorithm [2] with a maximum of 15 iterations. Filtered modulus and phase images and susceptibility maps were smoothed (band-pass filtering between 1 and 30 TRs) in the time domain before uncorrected activation maps ($p<10^{-10}$) were calculated with FSL. The GLM included the block-paradigm and its derivative, convolved with a double-gamma HRF and filtered in time with the same parameters as the functional data. Pre-whitening of the data was not performed.

Results

Temporal stability was improved significantly by correcting for global intensity variations. This was essential for efficient reduction of the background fields in the subsequent spatial filtering step. After initial global filtering in the time domain, all of the applied spatial filters were successful in removing low-frequency intensity variations and their application did not introduce temporal modulation. Removing slow phase modulations of external origin from the region of interest was important for successful quantification of baseline susceptibility maps. The relative phase filtering only retained information about dynamic changes in phase and, therefore, only relative functional susceptibility maps could be produced with this method. Figures 1-5 presented below result from an fMRI-dataset where a finger tapping task was performed and the dipole-fit reconstruction method was used. Filtered phase images revealed fine structural brain contrast (Fig.2). Activation induced $\Delta\varphi$ (%-change) maps and maps of the phase change estimated using forward field calculation [9], by replacing susceptibility with the modulus %-change, were investigated. Fig.2 shows the estimated $|\Delta\varphi|$-map overlaid on the filtered phase image. The measured $|\Delta\varphi|$-map is presented in Fig.3. Significant differences between Figs.2 and 3 suggest that activation-induced BOLD susceptibility changes are not exclusively encoded in the T2*-weighted image intensity. The comparison of estimated and measured $|\Delta\varphi|$-maps additionally served for optimization of the reconstruction process. Fig.4 presents an SPM derived from the magnitude data along with the positive and negative susceptibility SPMs overlaid on the negative QSM. Comparison of activation patterns in modulus (Fig.1) and QSM data (Fig.4-5) reveals remarkable similarity, in spite of differences between T2* (Fig.1) and negative susceptibility contrast (Fig.4). As expected, susceptibility decreases ($-\Delta\chi$) up to 7% on activation as a result of the BOLD-change in blood susceptibility, but this negative change coexists with positive modulation in neighbouring voxels (Fig.5). Also, as expected, the highest BOLD changes in modulus, phase and susceptibility were observed around veins. Filtering out this vascular contribution will be necessary for detection of phase changes in the parenchyma (1° predicted by [10]) and to quantify susceptibility changes with better spatial correlation to neural activity.

Conclusion

Quantitative susceptibility mapping was extended for use in functional imaging and activation-induced BOLD susceptibility changes were mapped at 7T. This offers the possibility of BOLD-fMRI related directly to a basic physiological quantity (magnetic susceptibility), limiting the dependence on pulse-sequence parameters. The proposed algorithm can be applied on any time-series, if phase information has been collected, and there is no need for hardware or acquisition modifications.

References: 1. de Rochefort et al., (2010) MRM 63:194; 2.Wharton and Bowtell, (2010) Neuroimage 53:515; 3. Schweser et al., (2011) Neuroimage 54:2789; 4. Sanchez-Panchuelo et al., (2010) J Neurophysiol 103:2544; 5. Pfeuffer et al., (2002) MRM 47:344; 6. Hagberg et al., (2011) Neuroimage, in press; 7. Hussein et al., (2007) Appl. Optics 46:6623; 8.Tomasi and Caparelli, (2007) JCBFM 27:33; 9. Marques and Bowtell (2005) Concepts MR 25B:65; 10. Feng et al., (2009) NeuroImage 47:540

Figure 1 Figure 2 Figure 3 Figure 4 Figure 5