Increased apparent T_2-sensitivity in BOLD fMRI using stimulated echoes

U. Goerke[1], P-F. van de Moortele[1], K. Ugurbil[1]
[1]CMRR/University of Minnesota, Minneapolis, Minnesota, United States

Introduction:

The origin of the stimulus/task-induced signal changes in spin echo (SE) fMRI is dynamic averaging due to diffusion in the presence of field gradients surrounding deoxyhemoglobin containing microvasculature. The same mechanism is expected to be operative in stimulated echoes (STE). Compared to SE-fMRI, however, STE-fMRI has the potential for larger diffusion weighting and consequently larger stimulus/task induced signal changes because of to the presence of mixing time T_M. This property of STE has previously been used to examine the effect of generating functional maps using externally imposed gradients [1]. In the presented study, functional signal changes due to vascular gradients were examined simultaneously for both SE and STE and were quantified as a function of the mixing time T_M.

Methods:

One male and two female volunteers participated in the study. The paradigm consisted of two blocks presenting a red flashing checker board for 30 s followed by a resting period of 39 s. Breaks of at least one minute were made between the functional experiments. The experiments were performed on a Varian 7T scanner using a surface radio-frequency coil. Anatomical images were acquired using an inversion-recovery Turbo-Flash sequence. The slices were oriented along the calcarine fissure. For fMRI, the primary spin-echo (PRE) and the stimulated (STE) echo were acquired after the second and the third RF pulse, respectively, in the STE sequence using an EPI-readout (FOV: 12.8 cm, acquisition matrix: 64 x 64, six slices, slice thickness: 2 mm, interslice distance: 2.5 mm, T_E = 60 ms, T_R = 6s). Spoiler gradients (b = 15 s/mm^2 for both echoes) were used to suppress gradient echoes. The mixing time, T_M, between the second and the third RF-pulse was incremented in subsequent functional experiments (T_M = 75 ms, 325 ms, 575 ms, and 825 ms). The series of experiments with the four different T_M-values was repeated four times. The data sets for each T_M-value were combined. Maps of signal changes which significantly correlate with the stimulus were calculated. Regions-of-interest (ROIs) in primary visual cortex were defined in each subject. The trial averages of signal changes in the ROIs were computed. A Monte-Carlo simulation was performed to compute relative signal changes as a function of T_M for capillaries with a radius of 3 µm. The physiological parameters of reference [2] were used. Contributions to signal changes due field distortions of neighboring vessels were considered.

Results:

In all maps, significantly activated voxels ($z > 3.08$) were found in the primary visual cortex. The activated regions detected with the primary and the stimulated echoes for the various T_M-values largely overlapped. Examples are shown in Figure 1.

Trial averages of ROIs in the primary visual cortex are shown in Figure 2. The time courses of the PRE over the various experiments were reproducible. The maximal signal change of the PRE was consistent with the value for diffusion-weighted spin-echo (SE) experiments [3]. The amplitude of the relative signal changes of the STE is larger than the PRE for the used T_M-values and steadily grows with increasing mixing time. The simulated signal changes (single data points in Figure 2) show the same trend as the experimental results.

Figure 1:
z-maps of a single subject (T_M = 825 ms)
yellow-to-red scale:
$3.08 < z < 6.0$
green-to-blue scale:
$-3.08 > z > -6.0$

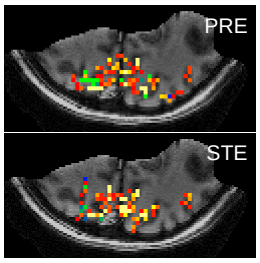
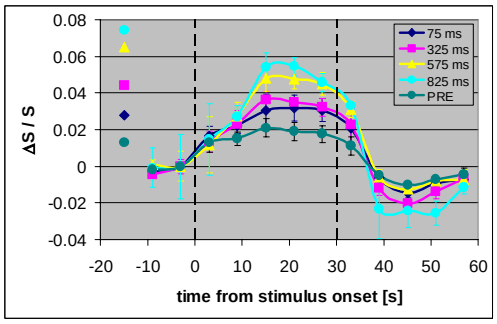


Figure 2:
Trial-averages of ROI in the primary visual cortex. Average of three subjects, error bars represent standard deviation of variation between subjects. Legends indicate corresponding T_M-value and the dashed lines start and end of stimulation. Single dots at the left represent simulated signal variations (same color-coding as for trial-averages).



Discussion:

STE is intrinsically less sensitive to inflow effects compared to SE, especially for longer T_M periods, and T_1-variations due to neuronal depolarization have been shown to be small [4]. Therefore, apparent T_1-effects are excluded as the source of the stimulus-induced signal changes in the presented study. Instead, supported by Monte Carlo simulations, it is suggested that, at a constant T_E, additional diffusion weighting due to T_M leads to larger functional signal changes. The STE-sequence also provides the option of using both the PRE and STE simultaneously for the generation of the functional maps, increasing statistical significance. The temporal "noise" characteristics of the approach remain to be examined. It is concluded that STE represents viable and potentially preferable alternative for microvascular based fMRI, especially for high fields, where T_1 increases and T_2 shortens for tissue water.

References:

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