Comparison of BOLD and CBV-weighted fMRI Studies using Multiple-refocused Spin-Echo

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Introduction

For BOLD-based fMRI brain mapping, spin-echo (SE) sequences can provide better spatial localization to brain parenchyma than the more widely used gradient-echo sequences. This is because in SE, the dynamic-averaging effect is more prominent for field inhomogeneities of smaller scales. The mechanisms of SE fMRI signal change, especially in the extravascular (EV) space, can be investigated using Carr-Purcell or multiple-refocused spin-echo (MSE) sequences [1,2]. It is usually assumed that the diffusion contribution to T_2 can be expressed by: $T_{2,\,diff}(n) \propto TE^3 / n^2$ or $R_{2,\,diff} \propto \tau^2$. By applying more refocusing π pulses (increasing n or decreasing the inter-echo pulse time τ) but keeping TE the same, the T_2 contribution to the EV BOLD signal change would be suppressed. The residue signal change was generally attributed to intravascular BOLD signal [1, 2], and possibly the T_2* effect due to the long SE-EPI readout [3]. To understand how effectively the π pulses could suppress the EV dynamic-averaging effect and also the spatial dependence of this refocusing effect, BOLD and CBV-weighted fMRI were studied at high spatial resolution using MSE sequences. With negligible IV signal, the T_2* effect contribution to the fMRI contrast which may be present in a SE-EPI sequence can also be evaluated.

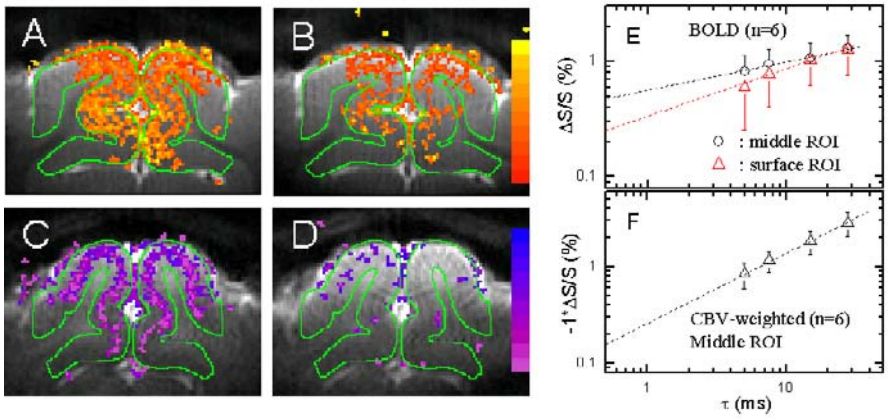
Materials and methods

fMRI experiments were performed on a 9.4T MRI (Varian) system. Twelve female adolescent cats were anesthetized and scanned using a surface coil. A coronal slice was chosen for fMRI study. A T_1 weighted image with 128×128 matrix size was obtained for anatomical reference. To ensure that the IV BOLD signal was minimal, the echo time TE was fixed to 60ms, much longer than the blood T_2 (~5-7ms) at 9.4T. Other imaging parameters were: 2×2cm^2 FOV, 2mm slice thickness, 2-segmented EPI with TR 1s/segment, and 96×96 matrix size which was zero-filled to 128×128 for reconstruction. Four MSE sequences were used with inter-echo time intervals τ = 28ms, 15ms, 7.5ms and 5ms (correspondingly, the number of π pulse is n = 2, 2, 4 and 6). The π pulses used were adiabatic full passage pulses [4]. Since adiabatic π pulses should be used in pairs, the time interval between the 1st π pulse and the excitation pulse (2nd π pulse) was 2 ms (30 ms) in the τ = 28ms sequence, while it was 15 ms (30 ms) in the τ = 15ms sequence. Four τ values were divided into two groups and scanned in an interleave manner: long τ (28ms and 15ms) and short τ (7.5ms and 5ms). For BOLD experiments (n=6), diffusion weighting of 20s/mm^2 to 300s/mm^2 were applied to further suppress the IV signal. The same parameters were used in CBV-weighted experiments (n=6) with a 10mg/kg dose of MION injection. BOLD and CBV-weighted studies were performed separately on different animals due to time restriction. Binocular visual stimuli consist of high contrast moving gratings. The stimulus paradigm is 60s control, 40s stimulation, and 80s control. In each study, 15 to 25 data sets were averaged for each τ value, and the total scanning time was about 4-5 hours. Signal fractional change maps were calculated with a minimal cross correlation coefficient of 0.3 and minimal cluster size of 4 pixels. ROI-based data analyses were performed in which two ROIs were drawn from the anatomic image: one at the surface of the cortex and the other at the middle of the cortex. Same ROI was used for all the τ images.

Results and discussions

The figures showed BOLD (A-B) and CBV-weighted fractional signal change maps (C-D) at TE=60 ms, but with two different inter-echo time intervals: τ = 28ms (A, C) and 5ms (B, D). The color bar indicated signal changes of 0.3% for red (blue) and 4% for yellow (purple). Large area of BOLD activation was observed for τ = 28ms at the gray matter area, as depicted by the green contour. With six refocusing π pulses, many activated pixels remained in Fig. B, though the activation size and the signal change both became smaller. In CBV-weighted experiments, the activation for τ = 28ms was strong and well localized at the middle layer of the visual cortex (C). At τ = 5ms the EV signal change was mostly suppressed with only a few activated pixels left (D). For the middle (surface) cortical ROI, the BOLD signal fractional change (proportional to ΔR_2) as a function of τ was shown in logarithm scale in Fig. E. Fitting the data to $\Delta R_2 \propto \tau^{\alpha}$ gave α = 0.25 for the middle ROI, and α = 0.43 for the surface ROI. For CBV-weighted results (F), the fitting gave α = 0.69 for the middle cortical ROI. The surface ROI was not analyzed for CBV-weighted experiments since there were few activated pixels.

Our results indicated that for BOLD, the additional π pulses removed the EV signal change more effectively at the surface large vessel area than at the middle cortex. In the parenchyma region (middle ROI), the refocusing effect of the MSE sequence is significantly different for BOLD and CBV-weighted fMRI signal changes. However in all cases, the suppression of the EV signal changes by the MSE sequence is not as effective as the expected power of α = 2 from the relation $R_{2,\,diff} \propto \tau^2$, especially for BOLD at the parenchyma region. The discrepancy is not likely caused by either the intravascular blood signal or the T_2* contribution in a SE-EPI readout. The IV signal was certainly eliminated in the CBV-weighted experiments. For BOLD, the MSE results with b = 20s/mm^2 to 300s/mm^2 were similar, indicating the IV signal was also negligible. Since same EPI readout was used for all the τ images, the T_2* contribution, if present, should be independent of the τ value. In the CBV-weighted results, the intercept approaches 0 when extrapolating to $\tau \to 0$ (Fig. F), indicating the T_2* effect contribution is negligible. The T_2* contribution should be even smaller in the BOLD case. The response (and the spatial dependence) of the BOLD and CBV-weighted signal changes to the MSE sequences reflected different EV dynamic averaging effects due to differences in the strength of the magnetic field inhomogeneities (and the vessel size) [4,5], and are currently under investigation.



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