Intravascular BOLD signal contribution to the fMRI ADC changes in the IVIM model regime

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Introduction

In the intravoxel incoherent motion (IVIM) model regime (usually $0<b<300$s/mm^2) [1], an apparent diffusion coefficient (ADC) increase in the parenchyma had been reported during brain activation and the response was found to be slightly faster than BOLD [2, 3]. The signal source of this ADC contrast was mostly ascribed to the functional blood flow and volume increase at the arterial side [2, 3]. However, it should be noted that although ADC is a measure of water mobility, other factors unrelated to water mobility may contribute to the ADC change as well. In particular, an elevation in the venous blood oxygenation level would effectively increase the relative weighting of the venous blood signal, thus elevating the measured ADC. This effect may not be ignorable, especially at low fields where the intravascular (IV) contribution to the BOLD signal change is significant. SE-EPI at 9.4T would be ideal for investigating this mechanism since the blood T_2 is short (~5-7ms), the IV contribution to the BOLD functional signal change is significant at short TE but vanishes at longer TE [4]. In this work the ADC functional contrast in the IVIM regime was studied using very short echo time (TE = 16ms) and compared to previous results of longer TEs (28ms and 60ms).

Materials and methods

fMRI experiments were performed on a 9.4T/31cm MRI (Varian) system. Seven female adolescent cats were anesthetized and scanned using a surface coil. A T_1 weighted image with 128×128 matrix was obtained for anatomical reference. A coronal slice was chosen for fMRI studies. A double echo EPI sequence was used with adiabatic half and full passage pulses. The imaging parameters were: 2×2cm^2 FOV, 2mm slice thickness, and 64×64 matrix size. To achieve a short TE of 16ms, 2-segmented EPI were used with 1s TR for each segmentation. The diffusion weighting gradients were placed on both sides of the second 180-degree pulse, and two b values of 2 mm^2/s and 200 mm^2/s were scanned sequentially, thus the effective TR was 4s for each ADC image. The binocular visual stimuli consisted of high contrast drifting square wave grating. The stimulation paradigm was 10 control (40s), 10 stimulation, and 10 control images. ~20 data sets were averaged. After averaging, images with the same diffusion weighting were separated, temporal-interpolation was performed, and then the ADC images were calculated. fMRI fractional change maps were calculated with a minimal cross-correlation coefficient of 0.3 and minimal cluster size of 3 pixels. Data analysis was based on two ROIs drawn on the anatomical image: one at the surface of the cortex and the other at the middle of the cortex. The same ROIs were used for ADC images and BOLD images with different diffusion weighing. The BOLD and ADC fractional changes were compared to those obtained previously at TE = 28ms and 60ms with similar experimental parameters.

Results

The relative signal change maps of b = 2 and 200s/mm^2 were shown in Fig. 1A and B for TE = 16ms and in Fig. 1D and 1E for TE = 28ms, respectively. Signal changes were consistently observed in the gray matter area, as depicted by the green contour. For TE=16ms, the strongest activated pixels for BOLD appeared at the surface large vessel area (Fig. 1A), and the activated pixels were mostly suppressed at b = 200s/mm^2 (Fig. 1B). Because the ADC change was related to the BOLD relative signal changes at the two diffusion weighting levels as: $\Delta ADC \propto \Delta S/S(b=2) - \Delta S/S(b=200)$, the ADC map (Fig. 1C) is similar to the BOLD map with b = 2 s/mm^2 (Fig. 1A), with stronger activated pixels located at the cortical surface. At TE = 28ms, large activated area was observed for both b = 2 and 200s/mm^2 (Fig. 1D and E). The signal changes in the ADC map (Fig. 1F) were larger at the middle of the cortex than at the cortical surface. Fig. 2 shows the relative ADC changes at two ROIs as a function of echo time. The relative ADC change increases with decreasing TE, more significantly at the cortical surface. The ADC changes of TE=16ms were ~7 (2) times that of TE=60ms for the surface (middle ROI).

Discussions

In an imaging voxel the ADC can be considered as a weighted average of the ADCs of different tissue and blood compartments. Any change in the relative compartmental size, such as blood volume dilation or blood oxygenation level change, would change the relative weighting and thus the measured ADC. Our results at 9.4T showed an echo time dependence of the functional ADC change in the IVIM regime. Since the T_2 of the arterial blood was similar to that of the tissue and independent of TE [5], the source of the TE dependence would likely be the venous blood signal. We have found that at 9.4T the IV contribution to the total BOLD signal change is significant at short TE but vanishes at longer TE (>50ms) [4]. With decreasing TE, the contribution from the venous blood signal change increases, leading to an increase in the ADC change, more significantly at the surface large vessel area. At TE = 60ms, there is negligible IV BOLD signal change, the small ADC change mostly comes from the change of arterial blood flow and volume [6]. At TE = 16ms, the dominant contribution to the ADC changes would be due to the IV BOLD effect. As a conclusion, our results indicated that an elevation in functional blood oxygenation level would increase the measured ADC. This contribution to the ADC contrast could be significant if the IV BOLD signal change is large, such as at lower fields.

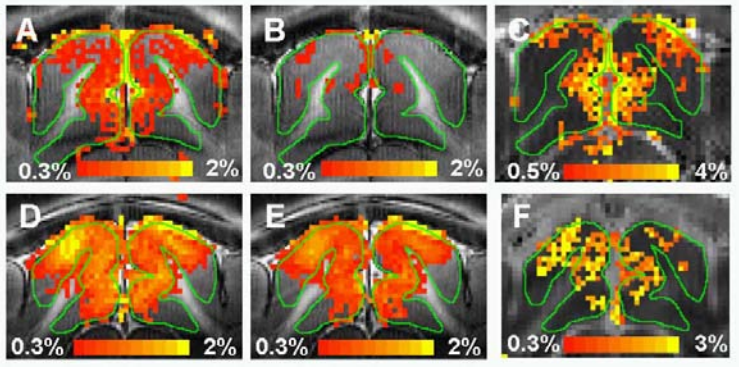

Fig. 1 *The fractional signal change maps for TE=16ms (A, b=2; B, b=200; C, ADC map) and TE=28ms (D, b=2; E, b=200; F, ADC map)*

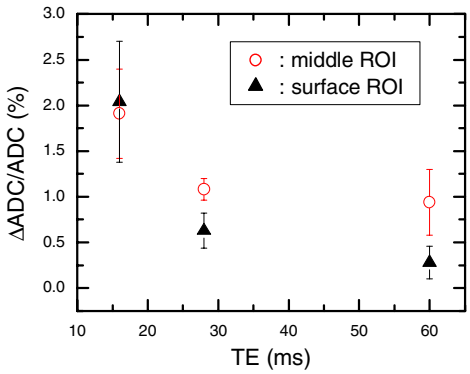

Fig. 2 *The fractional ADC change as a function of echo time*

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