ADC changes during cat visual stimulation measured by gradient-echo and spin-echo at 9.4T

T. Jin[1], P. Wang[1], M. Tasker[1], S-G. Kim[1]

[1]Brain Imaging Research Center, Department of Neurobiology, University of Pittsburgh, Pittsburgh, PA, United States

Introduction

BOLD contrast is widely used in functional MRI (fMRI) research. However, the spatial localization of BOLD signal can be distant from neuronal activity sites due to contamination of the signal from large veins, especially when using a gradient-echo. Recently, ADC contrast of brain water has been proposed as an alternative approach to detect task-induced signal change [1-3, 6]. However, the spatial resolution is limited in these human studies, and the signal source of the ADC functional changes is not well understood. In this work, ADC changes in cat brain during visual stimulation were measured at 9.4T, and the results of GE and SE were compared with BOLD results.

Materials and Methods

fMRI experiments were performed on a 9.4T MRI (Magnex/Varian) system. Nine female adolescent cats, weighting 0.8-1.5kg, were anesthetized as described previously and scanned with a surface coil [4]. For GE experiments (n=3), a pair of bipolar gradients were placed after the 90 degree slice-selective RF pulse for diffusion weighting. For SE experiments (n=6), a double echo EPI sequence was used with adiabatic pulses [4], and two unipolar diffusion gradients were placed on both sides of the second 180 degree pulse. The imaging parameters were: 2×2cm^2 FOV, 2mm slice thickness, 64×64 matrix size. The zero k-space line was shifted by 24 lines from the center to reduce TE. A T_1 weighted image with 128×128 scan matrix was obtained for anatomical reference. For GE (SE), an echo time of 18ms (28ms), a repetition time TR of 0.5s (1.2s) and three *b* values of 5, 200, 1000 mm^2/s (2, 200, 800 mm^2/s) were used, and the effective TR was 1.5s (3.6s) for three images. The binocular visual stimuli consisted of a drifting square wave grating (0.15 cycle/degree, 2 cycles/s). The stimulation paradigm was 20 (10) control, 20 (10) stimulation, and 20 (10) control images, and around 40 (20) data sets were averaged for GE (SE). After averaging, images with the same diffusion weighting were interpolated and shifted to take into account their different time origins. The small initial *b* value images were used as BOLD images. Two series of ADC images were generated for each experiment: one with *b*=5 (2) and 200 mm^2/s which were within the regime of the IVIM model [5]; the other with *b*=200, 1000 (800) mm^2/s which effectively measured the ADC changes from the tissue compartment while the intravascular signal is suppressed at these *b* values [3]. Cross-correlation coefficient (CCC) maps were calculated from a boxcar reference function with a minimal CCC of 0.3 and minimal cluster size of 3 pixels, unless otherwise noted. For each experiment, two ROIs (130-160 pixels) were drawn from the anatomic image: one at the surface of the cortex and the other at the middle of the cortex. The BOLD and ADC fractional changes were compared for the two ROIs.

Results and discussions

GE BOLD results of a representative cat are shown in Fig. 1a, and in 1b with higher CCC threshold (CCC>0.85). The green contour indicates the primary visual cortex obtained from the anatomical image. As expected, the largest signal change mostly occurs at the surface of the cortex. The ADC map obtained from small *b* values (Fig. 1c) shows somewhat different spatial characteristics: activated pixels are more scattered on the cortex, though part of them are still close to the surface. SE BOLD results of another cat are shown in Fig. 1d, and in 1e with higher CCC threshold (CCC>0.7). The largest signal change appears in the middle of the cortex, in agreement with previous results [4]. In contrast to the GE case, the ADC map from small *b* values (Fig. 1f) shows very similar spatial localization compared to BOLD (1e). The number of the activated pixels in Fig. 1b and 1c (1e and 1f) are similar, and their fractional change time courses are plotted in Fig. 2a (2b) for GE (SE). The time courses of the BOLD and ADC signals show similar patterns for both GE and SE, which is plausible because ADC changes within the IVIM model originated mostly from hemodynamic response to neuronal activation, similar to the BOLD case.

A positive ADC change during activation can be caused by an increase of blood flow and volume [1], or by a decrease of the magnetic susceptibility effect [6]. From the ROI (not shown) at the surface (middle) of the cortex, the calculated BOLD fractional signal change is 0.98 ± 0.22% (0.74 ± 0.23%) for GE (mean ± SD, n=3) and 0.56 ± 0.13% (0.67 ± 0.16%) for SE (n=6), while the ADC fractional change is 0.63 ± 0.35% (1.14 ± 0.32%) for GE and 0.65 ± 0.09% (1.03 ± 0.15%) for SE. Thus unlike BOLD, ADC changes are significantly higher at the middle of the cortex in both GE and SE, and the two sequences give very similar results. This suggests that the physical origin of the ADC change should be different from BOLD and not much related to the susceptibility effect which is more significant at the surface of the cortex. In both GE and SE cases, the signal to noise ratio of the ADC images calculated from the large *b* value pair is very low. No robust ADC changes can be detected consistently without further data post-processing. Moreover in the middle cortical ROI, BOLD fractional changes are almost identical: 0.48 ± 0.15% (0.47 ± 0.12%) at b = 200 (800) mm^2/s for SE (n=6), suggesting the ADC change is negligible. Thus the susceptibility effect-induced ADC change, caused by a coupling between the diffusion gradient and background susceptibility gradient [6], should be minimal at the middle cortical area. In conclusion, the ADC change we observed during activation, with highest changes occurring at the middle cortical area, is mainly caused by an increase of blood volume and flow. This agrees with the previous hypothesis that the signal source of ADC changes within the IVIM model regime mainly comes from small arterioles and capillaries of the arterial side when a small initial b value is used [2].

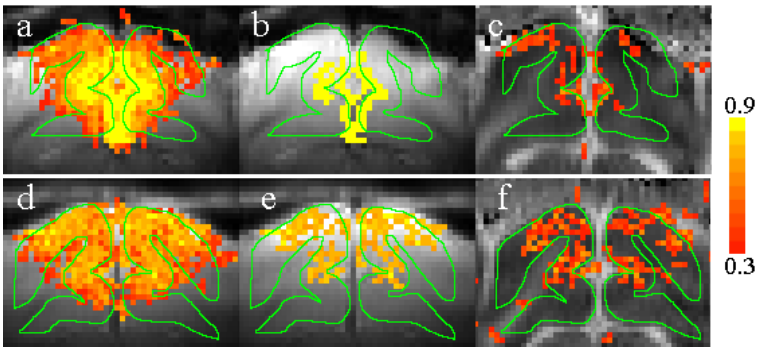

Fig. 1 BOLD and ADC cross-correlation maps from GE and SE

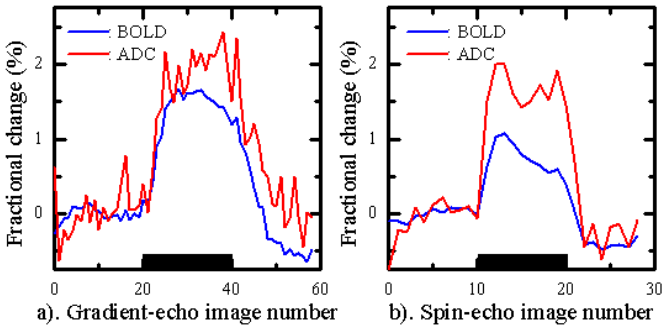

Fig. 2 BOLD and ADC fractional change time course from GE and SE

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