Spatial Characterization of Functional Activation Using BOLD, ADC and Perfusion Contrasts

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Abstract

Through spatial comparison of the activation extent among ADC, perfusion and BOLD contrasts, better understanding of the signal origins of these contrast mechanisms can be reached. It was found that despite a close relationship of the signal origins between the ADC and perfusion contrasts, significant spatial discrepancies remain between their respectively activated regions. In addition, both the ADC and perfusion activations showed significant spatial discrepancies with the BOLD activation, consistent with their distinct signal origins. We anticipate that the complementary information acquired from this multi-contrast analysis can provide much better characterization of the brain hemodynamics during activation.

Introduction

BOLD contrast is widely used for mapping brain activation attributed to its high temporal resolution and robust sensitivity. However, it suffers from coarse spatial co-localization to the true neuronal activity due to its non-selective sensitivity to the oxygenation level changes in vessels of all sizes. As an alternative, perfusion contrast using pulsed arterial spin labeling technique has been adopted to potentially provide better spatial localization to the capillaries, although the transit time limits its temporal resolution and the longitudinal recovery causes systematic errors. A second alternative, based on dynamic apparent diffusion coefficient (ADC) contrast sensitive to intra-voxel incoherent motions (IVIM), could robustly detect synchronized hemodynamic response during brain activation[1-4]. Given the relative early stage of its role in fMRI, and in addition to some early evidences of its arterial origin, the exact nature of such a contrast is under continued investigation. A comparison of ADC contrast with the established perfusion contrast is thus of high interest as it may lead to better understanding of cerebral hemodynamics during brain activation.

Methods

Six healthy volunteers were recruited and provided informed written consent forms. All experiments were carried out on a General Electric 4T MR scanner (GE Signa, Milwaukee, WI) with a shielded quadrature birdcage head coil. The stimulus paradigm was a block design using 30 sec of fixation followed by 30 sec of 8 Hz black and white radial flashing checkerboard. Four oblique slices (with 24 cm FOV, 64x64 matrix size, and 5 mm slice thickness) through the calcarine fissure were acquired sequentially from the superior to the inferior using a single shot gradient-recalled spiral acquisition.

To visualize the dynamic changes of the apparent diffusion coefficients, a temporally ramped isotropic diffusion-weighting scheme was used. Three *b* factors at 2, 114 and 229 s/mm^2 were cyclically varied along the time course. The initial small b factor at 2 s/mm^2 was used to reduce large vessel contaminations. A total of 210 time points were acquired in each run of 3.5 min at a repetition time (TR) of 1 s and echo time (TE) of 50 ms. A matrix of 64 x 64 was used with a FOV of 24 cm. The relatively long echo time was necessary to accommodate the weighting gradients. To reduce inflow contrast, the flip angle was set at 30^o. A total of 70 ADC time points were calculated by a monoexponential regression of the three data points in each cycle. The data with b = 2 s/mm^2 was used as a BOLD time series.

Perfusion weighted images were acquired using the multi-slice Flow-Sensitive Alternating Inversion Recovery (FAIR) scheme[5] with the FOCI inversion pulse (bandwidth =4000 Hz, pulse length = 16 ms). The selective inversion recovery (ssIR) and non-slice selective inversion recovery (nsIR) were alternated in an interleaved fashion. Two TIs, 1.2 s (perfusion I) and 1.4 s (perfusion II), were used. Other imaging parameters were: imaging slab = 20 mm, inversion slab = 40 mm, TE = 15 ms, TR = 3 s. A total of 35 time points of perfusion images were then generated using a pair-wise subtraction between ssIR and nsIR.

The dynamic time courses of BOLD, ADC and perfusion were then detrended and analyzed using a general linear model. Statistical significance maps were obtained from multiple linear regression algorithms. Activations from the ADC, perfusion and BOLD contrasts were then compared with each other. Average hemodynamic response was obtained from the activated regions of visual cortex. Since different subjects have different signal intensity levels, the inter-subject average time course was calculated from the weighted sum. The signal intensity ratio between the subject and a reference subject was selected as the weighting factor.

Results and Discussion

Figure 1 shows the respective activation among ADC, perfusion and BOLD activation maps from a representative subject. To keep the same number of activate pixels in each map, different Z thresholds were used. Spatial discrepancies exist among ADC and perfusion I, perfusion II, and BOLD. Comparisons were carried out for all subjects in the visual cortex systematically. The results showed that ADC-Perfusion I had a total overlap of 195 pixels, ADC-Perfusion II had 137. Thus the average overlap coefficient (overlap pixels divided by the activation pixels) between ADC and perfusion of all subjects decreases as TI increases. A spatial correlation shows that ADC has a higher correlation with perfusion I. This could indicate that ADC detects up-stream signal changes.

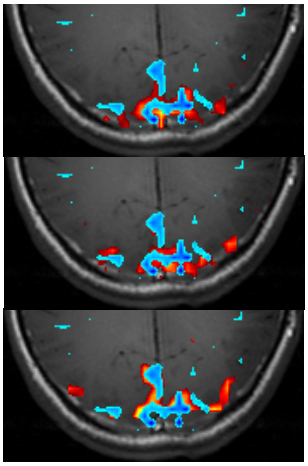

Figure 1. Activation maps comparison. To keep the same activation extent between the two maps, different Z thresholds were used. From top, ADC (blue, Z≥2.5) and perfusion I (red, Z≥4.4) with overlap of 19 pixels; ADC (blue) and perfusion II (red, Z≥4.3) with overlap of 17 pixels; ADC (blue) and BOLD (red, Z≥5.5) with overlap pixels of 23.

ADC and Perfusion activations showed significant discrepancies compared to the BOLD activation, suggesting their different signal sources. The faster response of ADC and perfusion verified that both of them could detect upstream vascular signal change, which means that ADC and perfusion are closely related. The signal percentage change for ADC is about 10% to 15%, which is very close to the perfusion signal change of 20% in our data. Both are much larger than a typical BOLD signal change of 5%, suggesting their sensitivity to the flow changes.

Conclusion

Analyses in both the spatial and temporal domains indicate ADC, perfusion and BOLD have differential sensitivity to brain activation, although ADC and perfusion share significant partial arterial or upper-stream signal contributions. This combined analysis can lead to better characterization of the signal origins of the ADC contrast. Such an improved understanding of the ADC contrast mechanism can lead to more efficient blood flow studies to better investigate the hemodynamics during brain activation.

Reference

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