Cortical Depth Dependence and Implications on the Neuronal Specificity of the Functional Apparent Diffusion Coefficient Contrast

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Introduction

The blood oxygenation level-dependent (BOLD) contrast is widely used in functional MRI because of its high sensitivity. However, its spatial specificity is limited by signal contributions from large draining veins, which are distant from the sites of neural activity. An alternative contrast mechanism based on functional changes of the apparent diffusion coefficient (ADC) was previously proposed [1,2]. Under mild diffusion-weighting sensitive to the intravoxel incoherent motion (IVIM) [3], the ADC contrast predominantly originates from the vasculature. Previous studies have shown that the ADC activation temporally precedes the BOLD activation, with overlapping but also spatially distinct activated regions, suggesting that it mainly originates from capillaries and upstream arterial networks, as opposed to the BOLD contrast, which originates from capillaries and downstream venous networks. Furthermore, by selecting an appropriate range of diffusion-weighting, the ADC contrast can be tuned to be sensitive to small vessel networks, which are more closely tied to the sites of neural activity, thus resulting in an improved functional localization.

High-resolution animal studies [4] have recently shown that when the venous blood contributions are minimized, the functional ADC changes are mainly caused by an increase in arterial blood volume and show a better spatial localization to the middle cortical layer than the BOLD contrast. However, the spatial specificity of the functional ADC contrast has not yet been demonstrated in humans at the cortical level. Here, we thus seek to investigate the cortical depth dependence and neuronal specificity of the functional ADC contrast in humans by performing simultaneous high-resolution BOLD and ADC imaging during visual stimulation.

Methods

Healthy volunteers were studied on a GE Excite 3T MRI scanner using an eight-channel RF coil. Simultaneous BOLD and ADC imaging was performed using a diffusion-weighted single-shot spiral gradient-echo sequence with three b factors of 2, 115, and 230 s/mm^2 cyclically interleaved within the same run [1,2]. A dynamic BOLD contrast was obtained by extracting the image volume time series acquired with b = 2 s/mm^2, whereas a dynamic ADC contrast was generated by fitting an exponential decay to the three image volume time series acquired at each b factor. An initial b factor of 2 s/mm^2 was chosen to reduce the signal contribution from large arteries with high blood velocity. Isotropic diffusion-weighting gradients [4] that have no cross-terms with the deoxyhemoglobin-induced background gradients were used to ensure that the measured ADC contrast is independent from the BOLD contrast.

Three coronal-oblique slices were acquired in the visual cortex with a field-of-view of 12.8 cm and a matrix size of 128×128, resulting in an in-plane resolution of 1×1 mm. Sensitivity encoding (SENSE) parallel imaging with a reduction factor of 2 was used to achieve such a high spatial resolution. Other parameters were: TR = 1 s, TE = 43 ms, flip angle = 60°, and slice thickness = 5 mm. High-resolution coplanar T_1-weighted images were also acquired for anatomical reference. The activation paradigm was a block design consisting of seven 30-second periods alternating between a fixation cross and a rotating and flashing checkerboard. Eleven runs, each containing 210 image volumes, were acquired and averaged to increase the signal-to-noise ratio (SNR).

The averaged image volume time series was linearly detrended to remove any slow drifts and temporally realigned using spline interpolation to account for the interleaved slice acquisition. BOLD and ADC time courses were generated as described above and correlated with a hemodynamic response function corresponding to the paradigm to derive Z-score maps, which were thresholded at Z>2 and with a cluster size of 5 voxels. Maps of the baseline ADC, functional ADC change (ΔADC/ADC), and BOLD signal change (ΔS/S) as well as their averaged profiles across the cortex were computed within a rectangular region-of-interest (ROI) selected along the parieto-occipital fissure (Fig. 1a). The first fixation block was used as the baseline, and the transitions between the fixation and stimulus blocks were excluded to compute the functional ADC change and BOLD signal change. All maps were interpolated to a resolution of 0.5×0.5 mm.

Results and Discussion

Representative results are shown in Figure 1. The BOLD activation map (Fig. 1b) shows extensive and widespread activation throughout the visual cortex, particularly along the sulci, due to contributions from large draining veins at the cortical surface that are distant from the sites of neural activity. In contrast, the ADC activation (Fig. 1c) is more localized and restricted to gray matter regions.

The ROI analysis shows that the baseline ADC (Fig. 1d,g) is significantly higher at the cortical surface because of contributions from large vessels with high blood velocity and/or cerebrospinal fluid with high ADC value. Conversely, the functional ADC change (Fig. 1e,h) is significantly higher in the deep cortical layers, whereas the BOLD signal change (Fig. 1f,i) is more widespread and varies much less significantly across the cortex. These results are in good agreement with previous animal studies [4] and demonstrate the cortical depth dependence and improved spatial specificity of the functional ADC contrast as compared to the BOLD contrast.

While these preliminary results are encouraging, our current implementation of ADC imaging is still limited by a low sensitivity and efficiency. Further work is currently underway to increase the SNR and adopt a single-shot ADC imaging technique [6] to improve both the efficiency and accuracy of the ADC measurements. With these technical advances, it is anticipated that a much improved functional localization can be achieved.

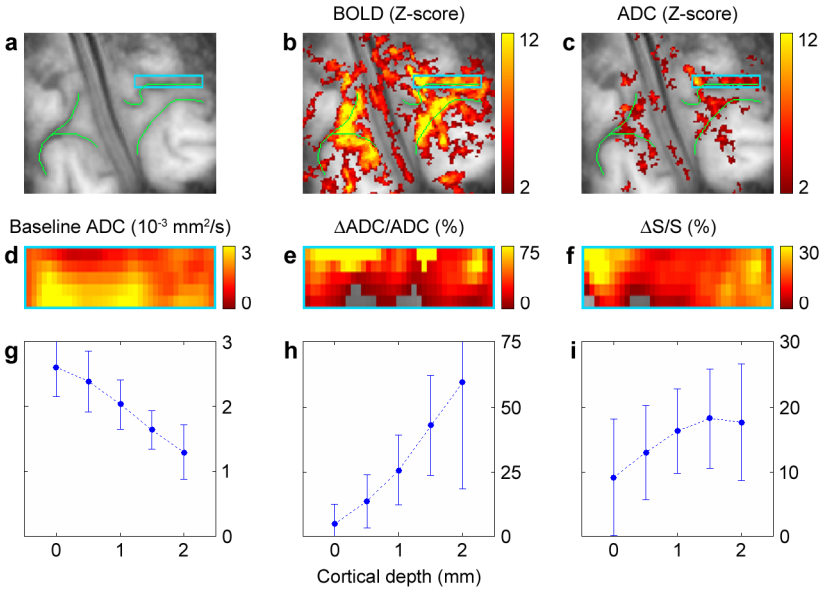

Fig. 1: Anatomical image with rectangular ROI selected along the parieto-occipital fissure (a). BOLD (b) and ADC (c) activation maps. Maps of the baseline ADC (d), functional ADC change (ΔADC/ADC) (e), and BOLD signal change (ΔS/S) (f) within the ROI, and their respective averaged profiles across the cortex (g,h,i).

References

1. Song *et al*. Neuroimage 2002;17:742–750.
2. Song *et al*. J Neural Eng 2004;1:32–38.
3. Le Bihan *et al*. Radiology 1986;161:401–407.
4. Jin *et al*. Magn Reson Med 2006;56:1283–1292.
5. Wong *et al*. Magn Reson Med 1995;34:139–143.
6. Song *et al*. Magn Reson Med 2007;57:417–422.

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