Anisotropy of the BOLD Response

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Introduction

Previous studies have shown substantial reductions in the BOLD response when the imaging sequence contains diffusion weighting (1). The intravascular compartment is particularly susceptible to diffusion gradients, as most of the signal is lost even at relatively low b-values. This is due to the high velocities of intravascular incoherent motion, as compared to true diffusion processes. The finding of a lower BOLD response during imaging with diffusion weighting, therefore, seems to indicate that a majority of the response stems from the intravascular compartment. This leads to the hypothesis that the sensitivity of the BOLD response to diffusion encoding may depend on local structural factors such as vessel size and direction. The purpose of the present study is to investigate the spatial distribution of diffusion-sensitivity, as well as whether the BOLD response arises from isotropic structures.

Methods

Three healthy subjects were investigated in a 3T Siemens Trio scanner, using conventional checkerboard visual stimulation (8 Hz reversal rate). BOLD-weighted imaging was acquired with a gradient-echo EPI sequence, TR/TE=240/30 ms, flip angle 30°, Matrix 64^2, isotropic resolution (3.1 mm)^3. A total of 180 frames were obtained, each consisting of 3 contiguous slices. For every slice, imaging was repeated with diffusion encoding in each of 6 spatial directions, with b=200 sec/mm^2 or b=500 sec/mm^2. A box-car paradigm was used, consisting of five 60-second periods each with equal duration of darkness and visual stimulation. The data was motion-corrected using SPM2 realignment, and correction for signal drift was performed using a 2nd degree polynomial. For further analysis, a new dataset was constructed using the frames obtained during the latter half of each activation period, corrected for the average baseline signal. The difference images (ΔBOLD) were analysed using a general linear model with b-value as one covariate and 5 variables representing the diffusion encoding direction. High values of an F-test assessing the combined affect of the direction variables were interpreted as an indication of anisotropy.

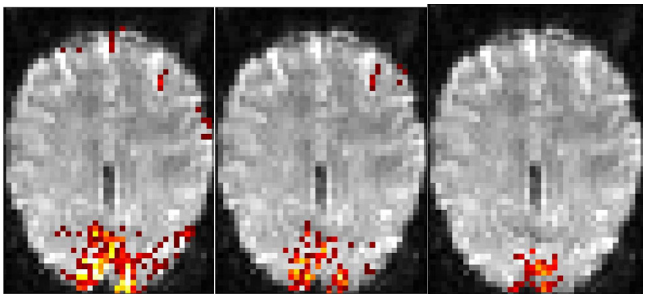

Fig A. BOLD visual stimulation	Fig B. Areas of signal decrease with b=200	Fig C. Areas showing effect of anisotropy

Results

A total of four experiments were obtained at b=200, and two at b=500. Activation maps from one subject are shown in Figs A-C. Activation-related signal increases were seen, as expected, predominantly near primary visual areas (Fig. A, thresholded at t>3.0) and had an average magnitude of 6.35% (range 5.98-7.15%). During measurements with low b-value, the BOLD signal change decreased by 43% (range 39-50%), whilst during the high b-value a decrease of 63% (range 57-69%) was seen.

The reduction in activation-related signal increase was seen throughout most of the area that contained significant activation related signal changes (Fig B, threshold t>3.0). In a few regions negative BOLD signal was seen during diffusion encoding. An effect of gradient direction was seen in a smaller part of the occipital cortex, but was never significant at a voxel level (F<1). Fig C shows the voxels with the top 5% incremental sum of squares due to inclusion of direction covariates in the design matrix. A quantitative measure of anisotropy was obtained by calculating BOLD attenuation factors for each direction. By diagonalization of the attenuation tensor, the fractional anisotropy could be calculated using a procedure analogous to the one used for conventional diffusion tensor imaging. Within the region of significant activation, the fractional anisotropy of the BOLD response was low, averaging 0.013 for the low, and 0.023 for the high b-value measurements. However, higher values of 0.035 and 0.057 were seen in areas corresponding to large extraparenchymal vessels (sag. sinus).

Discussion

The present study confirms earlier findings that the BOLD response is attenuated by relatively modest diffusion gradients, presumably due to the loss of BOLD signal from intravascular protons, and extends these findings by presenting a measure of the spatial distribution. While the intravascular BOLD contribution is always positive during transient states of increased venous oxygenation, the extravascular part may be negative depending on the level of CBV increase. Attenuation of the former may therefore lead to zero or negative overall signal change, as was actually observed in smaller regions. Calculation of BOLD attenuation and anisotropy maps yields information about the size and orientation of the vessels from where the signal arises.

1. Boxerman, J.L. et al. MRM 34:4-10 (1995)