Compartmental Selectivity of Diffusion Weighted BOLD fMRI at 4T

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INTRODUCTION

Conventional blood oxygenation level dependent (BOLD) functional magnetic resonance imaging (fMRI) techniques provide a non-invasive tool to monitor brain activity through the vascular response to changes in neuronal activity. While this technique provides a valuable tool to clinicians and researchers, contributions from large vessels distant from the site of neuronal activity limit the specificity of conventional gradient-echo BOLD imaging. A number of approaches have been introduced to reduce the contribution of large vessels in BOLD fMRI. Low levels of diffusion weighting have been used to suppress intravascular contributions to BOLD contrast [1,2]. Spin-echo acquisition has been used to selectively suppress the BOLD signal from the area surrounding large vessels. Imaging at higher field strengths can also help to suppress vascular contributions due to the shortened $T2^*$ of blood. The goal of this research was to systematically investigate the combined effect of these approaches to BOLD small vessel localization through an analysis of compartmental selectivity for the purposes of protocol design and development of new functional imaging methods.

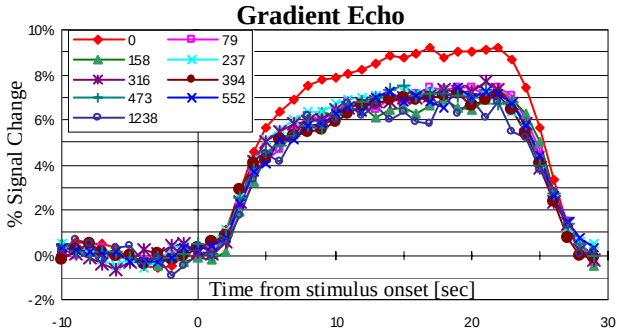
METHODS

Diffusion weighted single-shot gradient-echo images were acquired at 4T (GE Medical Systems, Milwaukee, WI) using a quadrature RF volume head coil in a subject under an IRB approved protocol. Imaging parameters were TR=1s, TE=68.6ms, flip angle=68°, matrix=64x64, FOV=24cm, seven coronal 5 mm slices with 5 mm spacing between slices, 380 temporal volumes. Nine acquisitions were performed using a different level of diffusion weighting (0, 79, 158, 237, 316, 394, 473, 552, 1238 sec/mm^2) for each. Additional data were acquired on the same subject using a diffusion weighted single-shot spin-echo spiral sequence, volume transmit coil, and four-channel visual array receive coil (Nova Medical, Wakefield, MA). Imaging parameters were the same as the gradient-echo session, except TE=69.6ms, flip angle=90°, six slices, and diffusion weightings = 0, 102, 202, 302, 402, 502, 602, 702, 1570 sec/mm^2. The stimulus paradigm consisted of nineteen 20 sec blocks alternating between a fixation cross and an 8 Hz reversing black and white radial checkerboard. Each acquisition began and ended with a fixation block.

Data were analyzed using custom software in MATLAB (Mathworks, Natick, MA). Student's *t*-tests were performed between the signals measured during the fixation and checkerboard blocks, assuming a six second hemodynamic delay, to generate functional maps for each diffusion weighting. Data ten seconds prior to and 29 seconds after stimulus onset were averaged to generate a mean time course for each diffusion weighting. An ROI was drawn on the non-diffusion weighted functional maps to include active ($t > 10$ for gradient-echo, $t > 5$ for spin-echo) voxels within the occipital lobe for the spin-echo and gradient-echo data. An ROI averaged time course was then calculated from the mean epoch for each diffusion weighting as show in Figure 1 and 2.

RESULTS

As shown in Figure 1, the percent signal change during activation was highest with no diffusion weighting and was attenuated to a consistent value for all levels of diffusion weighting applied. Figure 2 shows a similar behavior with the spin-echo data, however, the overall magnitudes of the responses are smaller.



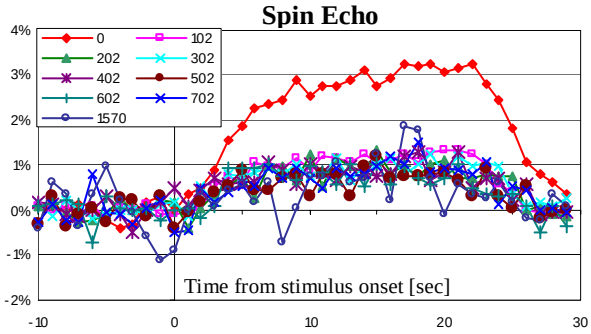


Figure 1 (Left) Gradient-echo mean signal time course for each diffusion weighting

Figure 2 (Right) Spin-echo mean signal time course for each diffusion weighting

DISCUSSION

This investigation of the response of the BOLD signal to a range of diffusion weightings revealed that increasing the diffusion weighting beyond a moderate level, perhaps even as low as 80 sec/mm^2, has no effect on the magnitude of the activation observed. Additional diffusion weighting decreases the SNR of the data thus reducing the detectability of the activation. These results were consistent between spin-echo and gradient-echo acquisitions. Additional investigation of diffusion weightings less than 200 sec/mm^2 may help to identify the minimum diffusion weighting necessary to suppress large vessel intravascular contributions.

To better understand the effects of the methods employed in this experiment on the signal contributions from various proton pools within the brain, we propose considering the brain from the perspective of four different proton pools: large vessel intravascular (IVL), small vessel intravascular (IVS), extravascular near large vessels (EVL) and extravascular near small vessels (EVS). For functional localization, we are most interested in the small vessel signals (IVS & EVS) since this signal will be closest to the source of neuronal activity. The large vessel signals (IVL & EVL) will likely contain signal from a larger area of cortex and be displaced from the actual area of neuronal activity thus reducing the specificity and accuracy of the functional activation maps.

The shortened $T2^*$ of blood at higher field strengths attenuates the intravascular signal raising the possibility that diffusion weighting is unnecessary. However, the observed reduction in the magnitude of the activation resulting from diffusion weighting demonstrates that some residual intravascular signal remains even at 4T, confirming the value of diffusion weighting strategies.

While diffusion weighting can be used to suppress the IVL signal, the EVL signal will remain in gradient-echo acquisitions, even with very strong diffusion gradients (Figure 1). Spin-echo acquisition can be used to refocus the field inhomogeneities near large vessels but not small vessels thus suppressing the EVL signal. The large difference in the diffusion-weighted signal between spin-echo and gradient-echo acquisitions (~ 1% vs. 7%) demonstrates the significance of the EVL effect present in gradient-echo imaging.

Through the application of diffusion-weighting gradients in spin-echo acquisition, we can suppress the signal from IVL, IVS, and EVL. The cost of this approach, however, is reduced BOLD sensitivity as the desired IVS is suppressed leaving only the EVS signal component. The small size of remaining signal (Figure 2) demonstrates the need to minimize diffusion weighting to maximize detectability. Contrast mechanisms that preserve both IVS and EVS may give better detectability without sacrificing specificity. Future research into alternate contrast mechanisms, such as very low diffusion weighting or ADC contrast may yield a contrast mechanism that is selectively sensitive to the signal in and around small vessels.

ACKNOWLEDGEMENTS AND REFERENCES

The spiral pulse sequence used in this experiment is based on a sequence developed by Gary Glover, Ph.D.

1. Song, AW. et al., *Mag Res Med*, 35, 1996. 2. Weingarten CAP. et al., *NMR in Biomed*, 11, 1998.