1 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 these techniques provide valuable tools 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 (DW) 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.

2 METHODS

Stimuli and Experimental Design

• Nine 20 second 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 for all exams were acquired from the same healthy subject recruited under an IRB approved protocol.

Imaging Parameters

• 4T MR imaging system with 40 mT/m, 150 T/m/s gradients. (GE Healthcare, Milwaukee, WI)
• Experiment A: Gradient Echo – High DW
  • Diffusion weighted single-shot gradient-echo/spiral imaging
  • 64 x 64, TR = 1 s, TE = 68.6 ms, Flip Angle = 68°, FOV = 24 cm, 380 temporal volumes
  • 7 Coronal slices (5 mm thick with 5 mm spacing between slices)
  • Diffusion weightings: 0, 102, 202, 302, 402, 502, 602, 702, 1570 sec/mm²
  • Diffusion direction: All three axes simultaneously
  • Volume transmit/receive head coil (Nova Medical, Wakefield, MA)
  • Common Parameters for Spin Echo Acquisitions:
    • Diffusion weighted single-shot spin-echo spiral imaging
    • 64 x 64, TR = 1 s, FOV = 24 cm, 380 temporal volumes
    • 6 Coronal slices (5 mm thick with 5 mm spacing between slices)
    • Volume transmit/receive head and four-channel visual array receive coil (Nova Medical)
  • Experiment B: Spin Echo – High DW
    • Diffusion weightings: 0, 79, 158, 237, 316, 394, 522, 1238 sec/mm², TE = 69.6 ms
    • Diffusion direction: All three axes simultaneously
  • Experiment C: Spin Echo – Medium DW, one direction
    • Diffusion weightings: 0, 26, 51, 76, 101, 126, 150, 200 sec/mm², TE = 41.7 ms
    • Diffusion direction: All three axes simultaneously
  • Experiment D: Spin Echo – Medium DW, Approx. isotropic, flow-moment nullled
    • Diffusion weightings: 0, 25, 50, 75, 99, 124, 149, 174, 199 sec/mm², TE = 87.5 ms
    • Diffusion direction: Approximately isotropic, flow-moment nullled
  • Experiment E: Spin Echo – Low DW
    • Diffusion weightings: 0, 7, 14, 21, 28, 35, 42, 49, 56 sec/mm², TE = 55.5 ms
    • Diffusion direction: Isotropic, flow-moment nullled

Data Processing

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 was also analyzed from the time point prior to and 29 seconds after stimulus onset to generate a mean time course for each diffusion weighting. An ROI was drawn on the diffusion-weighted functional maps to include active voxels (t > 10 for gradient-echo, t > 5 for spin-echo) 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 shown in Figures 1-5. Another ROI was drawn to include only voxels in the occipital lobe that were active (t > 3.6) at all diffusion weightings. The ROI averaged time course for this ROI is shown in Figure 6.

3 RESULTS

As shown in Figure 1, the percent signal change during activation was highest with no diffusion weighting and was attenuated to a fixed level for diffusion weighting as low as 25 sec/mm². Isotropic responses are smaller.

Additional investigation of moderate diffusion weightings shown in Figure 3 revealed that diffusion weightings of 25 sec/mm² and higher achieved consistent percent signal changes. Isotropic flow-moment nullled diffusion weighting yielded the same pattern in Figures 4 and 5. Figure 6 shows the mean signal course for only those voxels which were active at all diffusion weightings. The 7 sec/mm² time course shows a larger percent signal change than the higher diffusion weightings.

4 DISCUSSION

Initial 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/mm², has no effect on the magnitude of the activation observed. These results were consistent between spin-echo and gradient-echo acquisitions. Based on these initial findings, three additional spin-echo experiments were performed to study diffusion weightings less than 200 sec/mm² to help identify the minimum diffusion weighting necessary to suppress large vessel intravascular contributions. Results from diffusion weighting incremented from 0 to 200 sec/mm² (Figure 3) show that the activation was attenuated to a fixed level for diffusion weighting as low as 25 sec/mm².

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 refresh the field inhomogeneities near large vessels but not small vessels thus damping the EVL signal. The large difference in the diffusion-weighted signal between spin-echo and gradient-echo acquisitions (~ 1.5% vs. 7%) demonstrates the significance of the EVL effect present in gradient-echo imaging.

An experiment was then conducted to finely sample very low b-values. As seen in Figure 5, there is significant attenuation even at 7 sec/mm². Data were also analyzed to include only those voxels which were active (t > 3.6) at all diffusion weightings to prevent a bias towards any particular diffusion weighting. The results in Figure 6 suggest that diffusion weightings greater than 14 sec/mm² do not further attenuate the magnitude of the activation. Diffusion weighting decreases the SNR of the data thus reducing the detectability of the activation. Therefore using the minimum diffusion weighting necessary to achieve the desired proton mobility effect will maximize functional sensitivity.

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.

ACKNOWLEDGEMENTS & REFERENCES


[7] The spiral pulse sequence used in this experiment is based on a sequence developed by Gary Glover, PhD at Stanford University.