Investigating the Origins of the DfMRI Signal Using 4 Tesla

R. Waggoner[1], K. Tanaka[1], and K. Cheng[1,2]
[1]Laboratory for Cognitive Brain Mapping, RIKEN-BSI, Wako-shi, Saitama, Japan, [2]fMRI Support Unit, RIKEN-BSI, Wako-shi, Saitama, Japan

Introduction: Recent diffusion weighted fMRI (DfMRI) studies in humans (1-3) have been preformed at 3T. These studies have each observed an increase in the fractional BOLD signal change with increasing diffusion weighting (increased *b* value) during functional stimulation. The origin of this effect remains controversial with both cell swelling (1) and vascular sources (2,3) being offered as potential explanations. If the source of the increase in the DfMRI response with increasing *b* value is the result of cell swelling, going to higher field should not alter the effect. If the source is the cross-term effect (4), the increase of DfMRI response with increasing *b* value, should be enhanced. A third possibility is that with increasing b value, the intravascular BOLD response is suppressed and the DfMRI response becomes more biased to the tissue BOLD response. In the above-mentioned studies, it was assumed that a *b* value of 250-600 was sufficient to suppress the signal coming from the vessels, however there have been experimental results suggesting much higher *b* values are needed to suppress the venous blood signal (5). If this third possibility is the case, going to higher fields should suppress the DfMRI effect, because the T2 of venous blood decreases more rapidly with increasing field than the T2 of gray matter (6). At 4T intravascular BOLD signal should be effectively suppressed even at b=0, for a typical TE used in DfMRI studies. Here we report the results of an analogous human study using a higher magnetic field, 4T, in an effort to better understand the origins of the DfMRI signal.

Methods: The same Twice-Refocused Spin-Echo pulse sequence used by Le Bihan et al. (1) and Miller et al. (2) was used to acquire diffusion weighted fMRI data at 4T (Varian Inc., Palo Alto CA), with a single-shot EPI readout and homodyne reconstruction (4 over-scan lines). A 4-channel receive array coil was positioned to cover the visual cortex. Five slices, with a thickness of 5mm and 20x20cm^2 FOV (matrix=64x64), were positioned roughly parallel to the calcarine sulcus. Tr/Te= 2s/100ms. Seven subjects (2 female, 33±3yrs) viewed a radial flickering checker board (8 Hz) stimulus, with a paradigm of [24s off-(20s on-24s off)x8]. Five functional runs were acquired, one for each *b* value (b = 0, 600,1200, 1800, 2400). For each subject a Fixed-Effects analysis across *b* values was performed to obtain a single activation map, with a *t*-value threshold of 2.5($p \leq 0.013$). The BOLD percent signal changes for each *b* value determined from the voxels identified by the activation map.

Results: Figure 1 shows the average SE-BOLD percent signal change as a function of *b* value. The only average SE-BOLD change that was statistically different from the b = 0 value was the one at b =1800(p=0.01). The average signal changes for b = 0, 600, & 1200 are statistically equivalent to b=0(p>0.05). When compared with b = 2400, none of the other *b* values were statistically different. Thus our results indicate that at 4T the SE-BOLD response in the visual cortex is independent of the *b* value. In addition the trends shown in Figure 1 are consistent with recent results at 7T in the rat (7) and at 9.4T in the cat (8).

Conclusions: Our results support the notion that at 3T the SE-BOLD response with a Te=87-95ms contains a significant intravascular contribution which is increasingly suppressed with increasing b. While at 4T with Te=100ms, the SE-BOLD signal contains minimal intravascular contribution, even at b=0. These findings do not preclude the possibility that cell swelling may also contribute to the DfMRI response. However, under the experimental conditions presented here, there is no clear evidence of cell swelling.

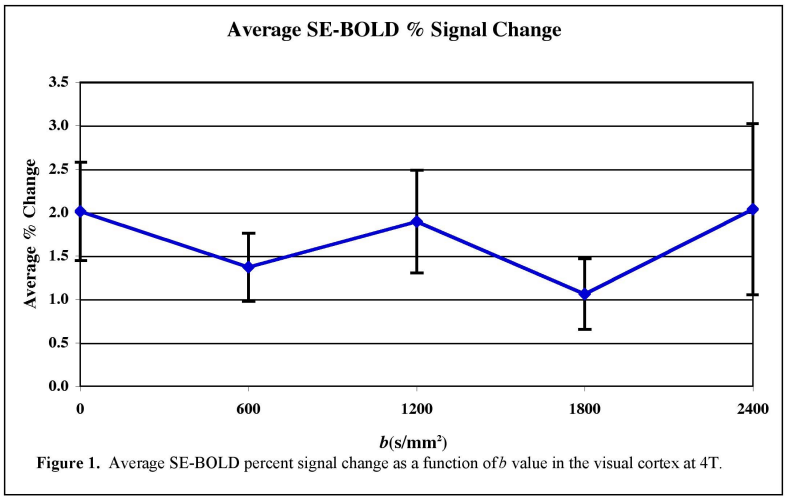

Figure 1. Average SE-BOLD percent signal change as a function of *b* value in the visual cortex at 4T.

References

1. Le Bihan, D. et al. (2006), "Direct and fast detection of neuronal activation in the human brain with diffusion MRI", *Proceedings of the National Academy of Sciences of the USA*, vol. 103, no. 21, pp. 8263-8268.
2. Miller, K.L. et al. (2007), "Evidence for a vascular contribution to diffusion FMRI at high b value", *Proceedings of the National Academy of Sciences of the USA*, vol. 104, no. 52, pp. 20967-20972.
3. Kershaw, J. et al. (2009), "A multi-compartmental SE-BOLD interpretation for stimulus-related signal changes in diffusion-weighted functional MRI", *NMR in Biomedicine*, vol. 22, no. 7, pp. 770-778.
4. Jin, T. and Kim, S.G. (2008), "Functional changes of apparent diffusion coefficient during visual stimulation investigated by diffusion-weighted gradient-echo fMRI", *NeuroImage*, vol. 41, no. 3, pp. 801-812.
5. Duong, T.Q. and Kim, S.G. (2000), "In Vivo MR Measurements of Regional Arterial and Venous Blood Volume Fractions in Intact Rat Brain", *Magnetic Resonance in Medicine*, vol. 43, pp. 393-402.
6. Yacoub, E. et al. (2003), "Spin-Echo fMRI in Humans Using High Spatial Resolutions and High Magnetic Fields", *Magnetic Resonance in Medicine*, vol. 49, no. 4, pp. 655-664.
7. Autio, J.A. et al. (2009), "Diffusion Weighted TE-dependent fMRI Signal in Rat Somatosensory Cortex at 7T", *ISMRM*, vol. 17, p 1572.
8. Yacoub, E. et al. (2008), "Deceases in ADC observed in tissue areas during activation in the cat visual cortex at 9.4T using high diffusion sensitization", *Magnetic Resonance Imaging*, vol. 26, pp. 889-896.