Diffusion-Weighted TE-dependent fMRI Signal in Rat Somatosensory Cortex at 7 T

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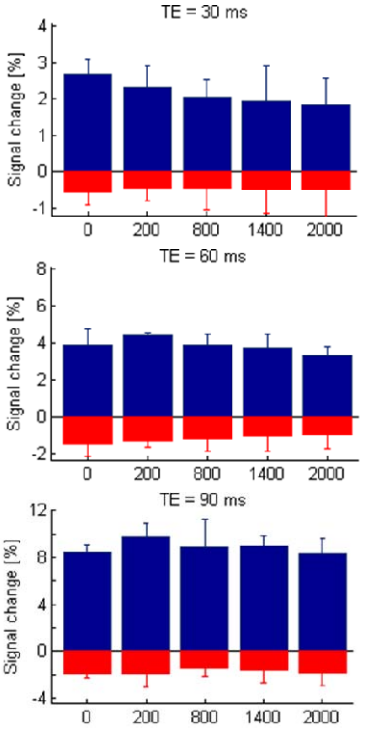
Introduction

There has recently been interest in applying diffusion-weighting (DW) during fMRI studies. It has been suggested that DW-fMRI signal courses might reflect vessel-size specific extravascular (EV) BOLD [1,2], cell swelling directly linked to brain activation [3] and changes in cerebral blood volume [4]. Verification of any these mechanisms might lead to a significantly enhanced understanding of the functional response. The aim of this study was to investigate the signal change dependency over a much broader range of imaging parameters and compare diffusion-weighted rat somatosensory stimulation results to previous human visual stimulation results [1, 2]. The experiments were performed on α-chloralose anaesthetised rats at 7 T with *b*-values 0-2000 s/mm^2 and echo-times of 30, 60 and 90 ms.

Methods

A somatosensory stimulation study was conducted on α-chloralose anaesthetised Sprague-Dawley rats (248-310 g). The animals were mechanically ventilated, arterial blood pressure monitored and blood gas sampled. The experiments were performed on a 7 T horizontal Bruker NMR spectrometer. Electric forepaw stimulation (0.3 ms pulse width, 2.0 mA current, 3 Hz frequency) had a block design of (60 s baseline) + [(20 s stimulation) + (100 s rest)] x 5 repetitions. The long rest period ensured the response returned to baseline before the next stimulus period. DW images were obtained with a SE EPI-sequence (TR 2 s, 64 x 64 matrix, 25 mm x 25 mm FOV) with motion-probing gradients on either side of the refocusing RF-pulse. Five diffusion-weightings (*b* = 0, 200, 800 1400 (x2) and 2000 (x3)) and three echo times (TE = 30 [n = 9 rats], 60 [n = 7] and 90 ms [n = 4]) were used. Activated pixels were identified and the intersection of two ROIs selected from the *b* = 200 and *b* = 800 s/mm^2 activation maps was formed. Voxels having a baseline apparent-diffusion coefficient (evaluated from the TE = 30 ms, b = 0 and 200 s/mm^2 data) that was clearly anomalous were removed from the intersection ROI. The final DW-time courses were obtained by averaging across ROI pixels, cycles and animals. The amplitudes of the *positive stimulus-correlated response* (PSCR) and *post stimulus-undershoot* (PSU) were calculated from the average of the signal time course in the intervals 10-20 s and 32-52 s, respectively, after the stimulus onset.



Results

Figure 1 shows the dependence of the PSCR (blue) and PSU (red) on *b*-value for all TEs. The error bars were calculated as the standard deviation across animals. Although the observed time-courses were qualitatively similar in shape as a function of diffusion-weighting (not shown), the PSCR tends to decrease with *b*-value for all TEs and *b*>200 s/mm^2. The PSCR increased from *b* = 0 to *b* = 200 s/mm^2 for the TE = 60 and 90 ms data. In Fig 2, the PSCR from one animal and each voxel in the selected ROI (green dashed lines) is compared to the mean across the ROI (black line). Even though this data set has TE = 90 ms and therefore the lowest SNR, the PSCR follows a similar pattern across *b*-values for all voxels. This pattern was consistently found for all TEs and animals and suggests that the selection process for voxels in the ROI is not crucial to the final result, and therefore the uncertainty across subjects in Fig 1 is mostly due to differences between the responses of individual rats to the experimental conditions.

Discussion

This is the first DW-fMRI study in rats with somatosensory stimulation. In earlier work it was suggested that the response might reflect vessel-size specific EV BOLD [1, 2], in which case the measurements acquired for this study should demonstrate clear changes to the response shape as either TE or the b-value is varied. As predicted by literature simulations (eg [5]), the amplitude of the response did increase markedly with TE. However, the response showed a much more subtle variation with *b*-value. The increase of the PSCR at high *b*-value found in previous DW-fMRI studies (eg [1-3, 6, 7]) was not observed for these experiments. Similarly, the PSU was not attenuated at high *b*-value as was observed for humans with visual stimulation. In fact, the qualitative shape of the response persisted for all *b*-values and TEs so it is likely that the signal changes at high *b*-value have the same origin (probably vascular-related [2, 4]) as those at lower diffusion-weightings. The contrary behaviour of the PSCR between *b* = 0 and 200 s/mm^2 for TE = 30 ms compared to that for TE = 60 and 90 ms may be due to the relatively short T2 of blood at 7 T [4].

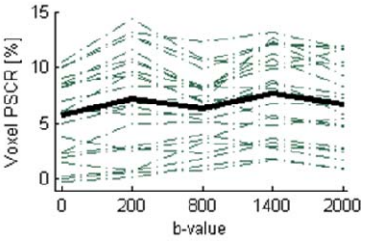


Figure 1.

References

[1] Kershaw *et al, submitted to NMR Biomed (2008)*; [2] Kershaw *et al, Proc ISMRM* 25 (2006); [3] Le Bihan *et al, PNAS* 103(21):8263-8268 (2006); [4] Jin *et al*, *Neuroimage* 41:801-812 (2008); [5] Fujita, MRM 46:723-734 (2001); [6] Yacoub *et al*, *Magn Reson Imaging* 26(7):889-96 (2008); [7] Miller *et al, PNAS* 104(52):20967-72 (2007).

Figure 2.