Diffusion weighted images in the cat visual cortex at 9.4 T reveal extravascular related ADC decreases during activation

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Background:

Previous studies in the human visual cortex (1-3) using diffusion weighted fMRI have suggested that the *apparent* water diffusion coefficient (ADC) decreases during neuronal activation. These changes have been attributed to transient cell swelling caused by either a shrinking of the extracellular space or by some intracellular neuronal process which precedes the hemodynamic response (3). Human studies, unlike animal studies, especially at lower magnetic fields, can be limited by signal to noise ratios, motion, and significant partial volume effects because of the lower spatial resolutions required for sufficient signal to noise in diffusion weighted images. Furthermore, signal changes in and around large veins are known to dominate the BOLD signal changes. Because of these reasons, the replication, reliability, and general utility of these findings in human studies at lower fields are limited. At high magnetic fields, signal to noise ratios increase, tissue signals are enhanced, and signal changes inside the blood are significantly reduced compared to lower fields. Higher magnetic fields and/or animal models can allow for more reliable and spatially accurate investigations of the fundamental physiological mechanisms associated with neuronal activation. Signal changes in the diffusion weighted BOLD fMRI time course can result from either intravascular or extravascular effects, as a result of oxygenation or flow related changes or possibly diffusion related effects. In this work we attempt to shed light on the origin of signal changes in the diffusion weighted fMRI time course in the cat visual cortex at 9.4 Tesla using high spatial resolutions and high b-values.

Methods:

Cats (n=3) were kept under isoflurane anesthesia throughout the experiment (1% in a N_2O:O_2 mixture of 70:30). Blood pressure, end-tidal CO_2 and body temperature were maintained at normal conditions. Visual stimuli consisted of binocular 30 s high-contrast square-wave moving gratings (0.15 cyc/deg, 2 cyc/s). All MR experiments were performed on a 9.4T/31cm (Oxford, UK) magnet. A 1.4-cm diameter surface coil for excitation and detection was used. A single coronal slice perpendicular to area 18 (crossing at Horsley-Clark AP2) was used for the functional study. Anatomic images were obtained using T_1-weighted 2D TurboFLASH. Hahn Spin echo BOLD images were acquired with different amounts of diffusion weighting using Stejskal-Tanner (S-T) gradients applied either simultaneously or separately along the 3 axes. Functional scans were acquired using b-values of: 1, 600, 1200, and 2400 s/mm^2. Image parameters were: Data matrix = 32 x 128, single shot EPI, field of view (FOV) = 0.8 x 3.20 cm^2. Slice thickness = 2 mm and TE/TR = 44ms /2 s. The in plane resolution was 250 x 250 μm^2. BOLD and ADC time courses were generated by selecting ROIs in the tissue and vessel areas and averaged over all cats.

Results:

Stimulus evoked Percent Signal (ΔS/S) changes were detected in the BOLD time courses at each of the different diffusion weightings in all animals. In each of the 3 cats, there was a slight monotonic (~ 20%) decrease ΔS/S from the tissue areas when increasing the b value from 1 to 1200 s/mm^2 (see Fig.1). The highest b-value (2400 s/mm^2) in *each* of the cats showed a return (or a relative increase) in ΔS/S to levels very near that of the b=1 s/mm^2 data. Data from the surface vessel ROI were, as expected, due to the low signal inside the blood at this high magnetic field, quite noisy and did not show any strong dependence on different b-values; however, the mean signal change did tend to decrease slightly with increasing b-values. Functional ADC time courses in the tissue and vessel areas (ΔADC/ADC) were also calculated based on the signal levels and changes from the different diffusion weighted images. In the tissue areas, when using a low b-value pair (1 & 600 s/mm^2) small relatively delayed increases in the ADC timecourse were observed (0.30 ± 0.08 %). When using the high b-value pair (1200 & 2400 s/mm^2) earlier and significant *decreases* (-0.45 % ± 0.3) were observed during activation in the ADC timecourses. Thus, on average, if all b-values are used, very small, if any, changes in ADC were observed during activation. In the surface vessel ROIs the ADC changes (with either low or high b–values) were small (and noisy), but did tend to increase during activation.

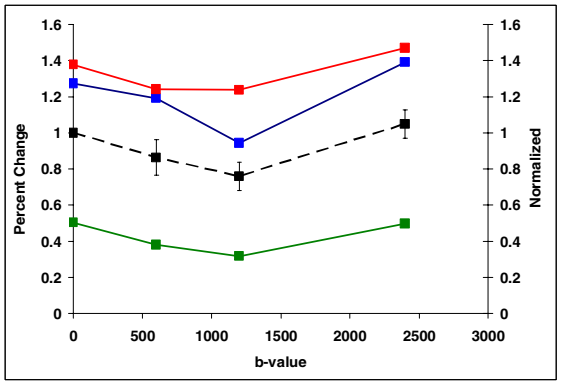

Fig.1 *BOLD signal changes as a function of b-value for 3 different cats (solid lines) and the mean normalized change for all cats (dashed line). (BOLD signal changes plotted on the left axis, and normalized change (average) on the right axis.)*

Conclusions:

Changes in the water ADC (observed via the BOLD signal) during activation can result from either intravascular or extravascular effects. In this work, when using the low b-value pair coupled with high magnetic fields, the intravascular effects are small (10 – 20 %), and small *increases* in the ADC during activation were observed. However, when going to even higher b-values (>1200 s/mm^2), where the intravascular effects are completely removed, the BOLD signal changes proceeded to recover and ADC *decreases* were observed in the tissue areas, possibly originating from a non-hemodynamic origin.

References: 1. Darquie et al, PNAS (2001) 2. Song et al, Neuroimage (2002) 3. Le Bihan et al, PNAS (2006).

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