Comparisons of diffusion-weighted and BOLD fMRI signals in the rat somatosensory cortex.
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Introduction
Diffusion-weighted functional MRI (DfMRI) has been shown to be sensitive to neural activation in the human brain. The DfMRI response in human visual cortex is characterized by earlier time-to-peak and return-to-baseline than the blood oxygenation level-dependent (BOLD) response [1, 2]. However, similar studies have been controversial in rodents [3, 4]. The goal of this study was to compare the DfMRI and BOLD signals in rat somatosensory cortex under hyperoxia without neuronal stimulation and forepaw electrical stimulation (ES).

Subjects and Methods
MRI experiments were performed on a 7T imaging system (Bruker, Ettlingen, Germany) using a dedicated surface coil. Twenty-nine male wistar rats were anesthetized with 1.5% isoflurane with air (30% oxygen). BOLD images were acquired using a Gradient echo-EPI sequence (TE/TR = 20/3000 ms), and DfMRI images were acquired using the diffusion-sensitized double spin echo-EPI sequence (TE/TR = 38.9/3000 ms, b=10, 250 or 1800 s/mm2). For both sequences, the following parameters were used: matrix size = 100 x 100, FOV = 32 mm, slice thickness = 1.2 mm, 3 slices. Anatomical images were acquired using multi-slice rapid acquisition with a relaxation enhancement (RARE): effective TE/TR = 60/2,500 ms, RARE factor = 8, matrix size = 256 x 256, FOV = 32 mm, slice thickness = 1.2 mm, 3 slices. Anatomical images were used for spatial correction. The experimental schedules were as follows:

**Experiment 1:** Five minutes after the beginning of the acquisition, air (30% oxygen) was replaced by 100% oxygen for 5 min, before switching again to air; total acquisition time was 15 min.

**Experiment 2:** 5 blocks of ES (2 mA, 7 Hz, 30 seconds) followed by a 30 seconds resting period was performed; total acquisition time was 5.5 min. To increase the SNR in higher b-value DfMRI, we measured 3 times for b=250 and 5 times for b=1800 and these were averaged after the experiment.

Data were spatially corrected using SPM5 (Welcome Trust Center for Neuroimaging, UK), and the signal changes were calculated using region of interest (ROI) of somatosensory cortex (Fig. 1) with the original program on Matlab (Mathworks, MA). We created the ROI according to the rat brain atlas [5].

Results

**Experiment 1:** The change from air to 100% oxygen significantly increased both BOLD and DfMRI signals (Fig. 2). We did not observe time delay between the BOLD and all DfMRI signals, but the amplitude of the BOLD response was significantly larger. No significant difference in the amplitudes of the DfMRI response corresponding to higher b-values (b=250 and b=1800) was observed.

**Experiment 2:** During ES, the amplitudes of the BOLD and highest DfMRI (b=1800) signals were similar (Fig. 3). The return-to-baseline of the DfMRI response was significantly faster, especially for b=1800 DfMRI response (Fig. 4).

Discussion

The differences between the BOLD and DfMRI responses point out different mechanisms. The reduced amplitude of the DfMRI response during hyperoxia compared to the BOLD (sharing the same time course) results from a residual T2 effect (no diffusion change) [2]. In contrast, the same amplitude and the early return-to-baseline of the DfMRI response compared to BOLD suggest a genuine diffusion component (on top of the residual T2 effect) that links to neural activity. However, the onset of the DfMRI response was not significantly earlier than the BOLD as in earlier human study [1,2].

References