Time course of transient changes of the apparent self-diffusion coefficient during task activation

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Motivation

It was previously reported that the apparent self-diffusion coefficient (ADC) decreases during stimulation [1, 2]. High diffusion weighting is required for a sufficiently sensitive detection of the subtle changes of the self-diffusion coefficient. Diffusion-weighted imaging is inherently sensitive to motion such as cardiac-related pulsations. It was demonstrated that in single-shot DTI experiments the variability of quantities derived from the diffusion tensor was reduced using ECG-triggered acquisition [3]. To reduce signal instabilities ECG-triggering was implemented in the stimulated-echo sequence.

Methods

Six female and four male subjects were investigated. A visual paradigm consisting of 30 blocks of 42 s pseudo-rotating red *L*'s followed by 38 s of fixation was presented.

The experiments were performed on a 3T Bruker Medspec scanner. Anatomical images were recorded using MDEFT. In the fMRI experiments, the diffusion-weighted primary (*pr*) and the stimulated (*st*) echoes of a three 90°-pulse sequence were acquired [2]. The parameters were: 5 slices oriented parallel to the sulcus calcarinus, field-of-view: 22.4 cm, slice thickness: 5 mm, interslice distance: 6 mm, acquired matrix: 64 x 64, echo time: 56 ms, echo position: 30%, diffusion gradients: 36.4 mT/m, duration of the gradient pulses: δ = 14 ms, diffusion times: Δ_{pr} = 15 ms, Δ_{st} = 84 ms, *b*-values: b_{pr} = 210 s/mm^2, b_{st} = 1470 s/mm^2. fMRI experiments were ECG-triggered. The acquisition of each slice was started 380 ms after the R wave. The repetition time (T_R) therefore varied between 5 times 650 and 5 times 1100 ms depending on the cardiac rate [50-90 beats/min]. The exact time points of data acquisition and the onsets of stimulation and rest periods were recorded and stored along with the image data for further processing.

The images of the primary and stimulated echoes were spatially smoothed using a Gaussian filter with half-maximum-half-width, σ, of 0.8. The apparent self-diffusion coefficient (ADC) was then calculated from the ratio of the stimulated over the primary echo images. Potential variations of the initial magnetization S_0 and T_2-relaxation are thereby eliminated. The time courses were baseline corrected with a width of 160 s. No further spatial smoothing or filtering was performed. The onsets of the stimulation and rest periods were calculated relative to the time points of data acquisition of each slice separately resulting in an apparent jittering of the onsets and durations of stimulation and resting periods. *Z*-maps were then calculated from the diffusion time courses using a boxcar design function (LIPSIA software package [4]). A *z*-map of a single subject is shown in Figure 1. Only clusters with more than two voxels are displayed.

For all ten subjects, regions-of-interest (ROIs) were marked for $z < -2.33$ ($p < 0.01$) in the visual cortex. Trial averages were calculated from the diffusion time courses in the marked ROIs. Time courses with a noise-to-signal ratio of more than 5% were omitted. The trial averages were binned with a temporal resolution of 1 s (Figure 2). A spin-echo BOLD-sensitized data set (T_E = 75 ms, T_R = 1 s, 6 stimulation blocks) of a single subject was statistically analyzed using the same procedure as for ADC data sets. The BOLD signal trial average was calculated from a ROI in the visual cortex showing significant activation, $z > 3.1$ (Figure 2).

Results and discussion

Using ECG-triggered acquisition the average standard deviation of temporal signal instabilities in the ADC time courses were reduced to the level of the in-plane noise-to-signal ratio of 3% of the stimulated echo. Spatial and temporal filtering could therefore be omitted maintaining a level of significance comparable to untriggered experiments with filtering. In nine out of ten subjects significant decreases of the apparent self-diffusion coefficient ($z < -2.33$, $p < 0.01$) were found in the maps (Figure 1). In Figure 2, the diffusion coefficient trial average of the marked ROIs of all subjects and the spin-echo BOLD trial average of a single subject are plotted. The orange box represents the stimulation period. The dashed line marks the delay of the maximal signal change of the BOLD response relative to the stimulus onset. The change of the diffusion coefficient reaches the plateau before the BOLD signal maximum. This finding suggests that the detected changes of the diffusion coefficient take place in the extravascular compartment indicating that changes in the ADC may probe neuronal activity more directly than the BOLD effect.

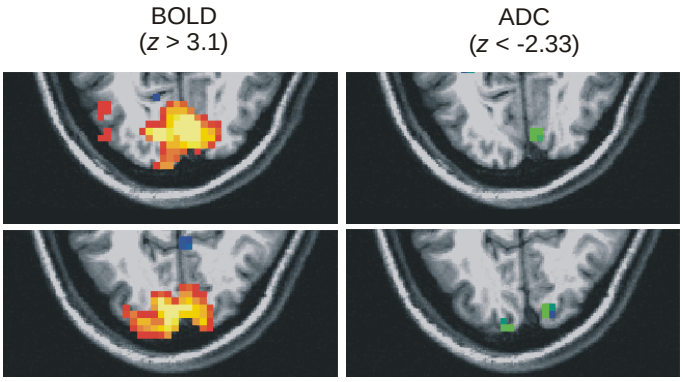

Figure 1: z-maps (two neighboring slices) of a single subject

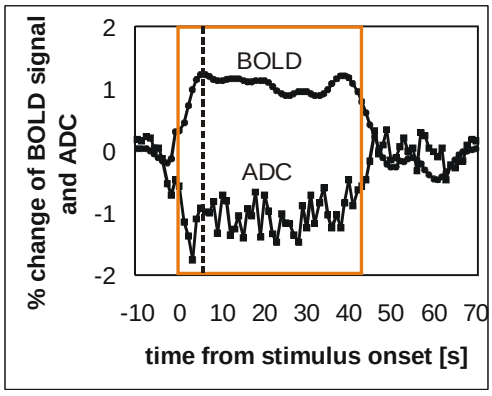

Figure 2: BOLD (1 subject) and ADC (ten subjects) trial averages

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