Functional MRI in the rat at 9.4 T and 16.4 T

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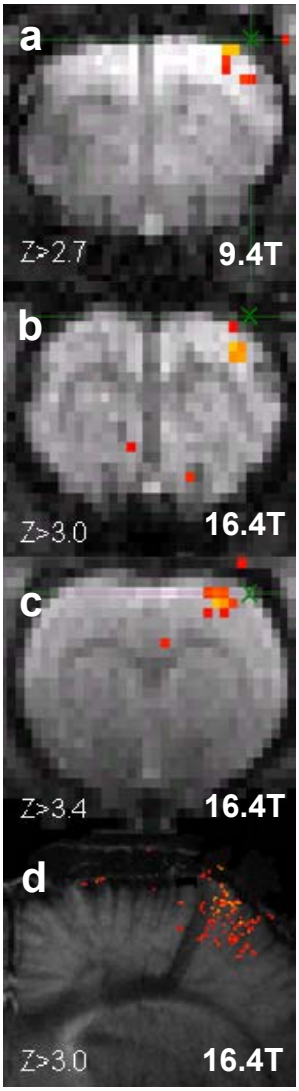
Introduction

Functional MRI (fMRI) in animals at high magnetic fields keeps expanding our knowledge about the basics of thinking and the fMRI-signal itself. Yet, until the signal to noise ratio in MRI depends linearly on the magnetic field strength and calls for even stronger magnets for the detection of even smaller anatomical details, the relation between the functional MR-response and field strength can only be approximated with complex models. In this study the blood oxygenation dependent (BOLD) effect was measured and compared at 9.4 T and 16.4 T in the same animal with segmented gradient-echo (GE) and spin-echo (SE) echo planar imaging (EPI) sequence using optimal echo times for the respective field. It will be demonstrated with high resolution activation maps that 16.4 T allows for a 50 µm in-plane accuracy and for an 8 s temporal resolution without the use of cryo-coils or coil-arrays.

Methods

Experiments were performed on a 16.4 T horizontal bore Bruker/Magnex animal scanner and on a 9.4 T Siemens human system with head gradients. Two, geometrically identical, custom built quadrature surface coils with 2.2 mm loop diameter were used for comparison between the BOLD-signal on 700 and 400 MHz, respectively. The preamps and T/R switches for these experiments were also homebuilt [1]. The high resolution fMRI datasets were acquired with a parallel conductor surface loop coil of 1 cm diameter [2]. Data substantiating the arguments and conclusions presented here were collected from two male CD rats of 450±20g. Animals used for sequence and method development are not counted. Anesthesia for the BOLD-experiments on different fields was induced with a 1.5 g/kg i.p. bolus of Urethane [3]. This form of anesthesia simplified the transportation of the animal, the handling and the monitoring system between the two magnets by rendering continuous administration of a gas or fluid drug unnecessary. For high resolution fMRI a Ketamine/Medetomidine bolus of 60/0.4 mg/kg was administered i.p. to induce anesthesia. Targeting maximum BOLD-response the state of the animal after 1.5-2 hours was maintained by starting continuous i.p. infusion of 36 mg/kg of α-Chloralose. Body temperature, breathing rate, pulse and blood oxygenation were monitored non-invasively and were maintained between the normal physiological limits. Echo times for the EPI sequences were set equal to the T_2* and T_2 relaxation times for the GE and SE experiments, respectively. Measurement of the relaxation times in the rat somatosensory cortex at the 9.4 T were performed prior to fMRI and also independently in another animal. The values at 16.4 T were determined in an independent comprehensive study, which will be presented elsewhere. A simple fMRI block-design was used employing rest phases followed by electrical stimulation of the forepaws with 2 mA / 11 Hz / 300 µs pulses trains. Activation maps for field comparison were calculated for Z>1.6 and p<0.03 using high- and low-pass filtering and spatial smoothing. For the high-res maps Z>2.3, p<0.01 and high-pass filtering was applied.



Results

Echo times were set to 20 ms for GE and 38 ms for SE-EPI at 9.4 T and 15 ms for GE and 28 ms for SE-EPI at 16.4 T, respectively. In the figure on the right 400x400x1000 µm activation maps are presented as overlay on the mean average of the timeseries. The BOLD-effect was calculated taken the sum over all activated voxels as percentage change between activated and resting states: 5% - GE@9.4 T; 7% - SE@9.4 T; 7% - GE@16.4 T and 6% - SE@16.4 T. GE-EPI images at 9.4 T (a) and 16.4 T (b) are qualitatively similar, though the activation map in (b) includes significantly more activated voxels and therefore it was thresholded at a higher Z-score. Comparing SE with GE images we observe that the signal cancellations at the edge makes the rat brain seem smaller in GE-images. The green cross indicates a voxel on the surface, which is dark due to susceptibility effects in (a) and (b). The activation map in (c) has very good quality indicated by the Z-threshold. The activated region is in every case inside the somatosensory area, but in (c) the specificity of the BOLD to the cortical layer-4 is apparent. In (d) a 50x50x1000 µm GE-EPI activation map is overlayed on the high quality timeseries average image. Timeseries of single activated voxels show a BOLD signal change between 20 and 50%.

Conlcusion

Good quality GE and SE-EPI were acquired at 9.4 T and 16.4 T. GE-EPI images are dark in surface regions of the brain and therefore care should be taken by referencing and registering the GE-based activation maps. The experiments presented here showed no substantial differences in the BOLD-signal change between 9.4 T and 16.4 T. However, timeseries can be better fitted to the block-design at the higher field, presumably because of the better sensitivity. This better sensitivity was demonstrated by the acquisition of activation maps with unprecedented spatial resolution in combination with a good temporal accuracy by using a simple surface coil.

References

[1] Shajan et al., Proc. ISMRM 2009. [2] Doty et al., NMR Biomed. 2007; 20:304-325 [3] Huthunen et al., Neuroimage 2008; 39(2): 775-785