TurboCRAZED BOLD imaging detects specific activation in the rat brain after somatosensory stimulation at 16.4 Tesla

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Introduction

Studies on humans at clinical field strengths have shown that the blood oxygen level dependent (BOLD) effect is increased in images acquired with pulse sequences detecting intermolecular multiple-quantum coherences (iMQC). Recently, hyperoxia-induced global BOLD contrast was observed in anesthetized mice [1] and rats [2] with the novel iMQC-imaging sequence TurboCRAZED. The aim of this study was to adapt TurboCRAZED for longitudinal fMRI with somatosensory stimulation on rats under extensive physiological monitoring at 16.4 T, and to detect specific activation with iMQC-imaging in animals.

Methods

Experiments were performed in a 16.4 T small animal scanner equipped with a strong (1 T/m) gradient system. A 22 mm transceiver loop coil and a homebuilt preamplifier were used. Medetomidine-anesthesia was applied, which allows for longitudinal fMRI studies [3]. Catheters were introduced in the tail artery for blood sampling and in a tail vein for infusion of the narcotic. Two platinum-iridium electrodes were inserted subcutaneously into one forepaw. During fMRI thermoregulation was provided, breathing rate and concentration changes in the exhaled gas were continuously monitored. Blood was sampled before every experiment and analyzed for blood-gases, pH and electrolytes to ensure homeostatic conditions. Somatosensory stimulation was achieved by a train of 300 µs long and 2 mA strong electrical pulses applied with a rate of 3 Hz through the electrodes in the forepaw. The original single slice version of TurboCRAZED selecting intermolecular double-quantum coherences was used [1]. This implied a mandatory four-step phase cycle, which prolonged experimental time by a factor of four. Therefore, sequence parameters had to be adapted to provide an acceptable time resolution for fMRI. The 1.6 x 1.6 x 0.3 cm^3 FOV was sampled in a 64 x 64 x 1 matrix, corresponding to an isotropic in-plane resolution of 250 µm and a slice thickness of 3 mm. The acceleration factor of the turbo spin echo readout was R = 32 and the effective echo time was 62 ms. A full volume was acquired every 48 seconds. Fig. 1 shows the experimental protocol, with a boxcar design of 2 x 4 min stimulation periods. During 36 minutes 45 volumes were acquired. The correlation length, the parameter which determines the structural weighting of iMQC-image contrast, was set to 165 µm. Uncorrected activation maps with a significance threshold of p=0.01 were calculated with the FEAT-utility of the FSL-software [4] from motion corrected and spatially smoothed TurboCRAZED images. The model function for fitting contained the Gaussian weighted stimulation block-design and its temporal derivative.

Results

Specific activation was detected with TurboCRAZED (Fig. 2) and the activated region could be tentatively assigned to the primary sensory cortex [5]. Z-scores in Fig. 2 are all above 2.3 and no significant activation in other regions was detected. The intensity timecourse of the most significantly activated voxel is shown with the model function in Fig. 3 (the first five images in timeseries were omitted by the fit). BOLD caused an intensity change of up to 6%. Evolution of the exhaled CO_2 was fairly constant in all experiments, with only a few transient changes, as in the case shown in Fig. 4.

Conclusion

We reported here the acquisition of the first stimulus-related BOLD activation maps in anesthetized animals using TurboCRAZED. Future studies with the presented setup are planned to investigate how the variable structure-weighted contrast mechanism of iMQC-imaging affects the BOLD contrast.

References

[1] Schneider and Faber, MRM 60:850 (2008), [2] Balla et al., Proc. ESMRMB Valencia (2008), [3] Weber et al., NeuroImage 29:1303 (2006), [4] Smith et. al., Neuroimage 22:208 (2004); [5] Paxinos and Watson, The Rat Brain (2007)

Figure 1: Stimulation paradigm: Blue – images; Green – stimuli.

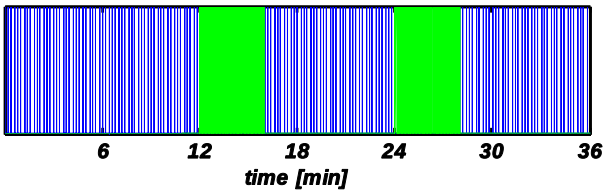

Figure 2: Activation map of a 3 mm slice in the rat brain.

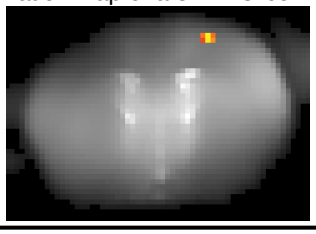

Figure 3: Intensity timecourse (red) and model (blue).

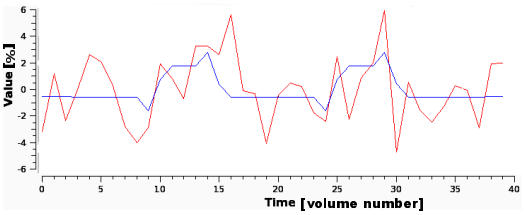

Figure 4: Relative timecourse of the exhaled end-tidal CO_2.