3D CBV-weighted Functional MRI of the Rat Brain with High Spatial and Temporal Resolution Using Half-Fourier Gradient Echo EPI

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Introduction

Whole-brain fMRI coverage is of fundamental importance to allow a broader understanding of neuronal pathways and functional brain connectivity. The use of small animals has significantly advanced our understanding of complex brain processes, such as learning and plasticity. However, few whole-brain functional MRI studies have been performed in small animals, partly due to the need for simultaneous high temporal and spatial resolution. The recent and progressive availability of high field imaging systems equipped with excellent gradient performance has enabled acquisition of high-resolution images at a rate conducive for functional imaging. In this study, we employ a 3D echo-planar imaging sequence to obtain CBV-weighted fMRI of the whole rat brain at 300x300x800 microns, with a temporal resolution of about 3 seconds.

Methods

Adult male Sprague-Dawley rats (n=5) were anesthetized with halothane, orally intubated and given venous and arterial lines. Two needle electrodes were inserted into each forepaw. The animal was placed on a warm water pad to maintain body temperature, and a bite bar and ear pieces were used to prevent head movement. Expired CO_2, rectal temperature, and blood pressure were continuously monitored, while blood gases were measured and maintained at normal levels. Anesthesia was switched to an α-chloralose infusion for imaging (1), and each rat was injected with 20 mg/kg iron oxide to obtain CBV contrast (2).

Imaging was performed on an 11.7 T/31 cm magnet (Magnex Scientific, Ltd., Abingdon, UK) interfaced to a Bruker Biospec-AVANCE console, and equipped with a 9 cm shielded gradient set capable of providing 450 mT/m within 75 µs rise-time. Excitation was provided by a home-built 70 mm ID birdcage coil, while a home-built rectangular surface coil (2x3 cm) was used as a receive coil. A 3D gradient-echo EPI sequence with the following parameters was used: FOV 1.92 x 1.92 x 2.56 cm, matrix size 64 x 40 x 32, nominal resolution 300 x 300 x 800 µm, effective TE 5 ms, BW 333 kHz, TR 100 ms, FA 15°. A complete 3D image was acquired every 3.2 s. Half-Fourier reconstruction was used to minimize the length of the acquisition and shorten the echo time. The stimulation paradigm was 50 images during rest, 25 during stimulation (3 Hz, 2 mA), and 50 during rest. Correlation maps were calculated using STIMULATE (Univ. of Minn.). Thresholds for activation were set at 0.3, with a cluster of at least 4 pixels.

Results

Excellent image quality was obtained using the 3D EPI sequence, with minimal spatial distortion and acceptable blurring from the half-Fourier reconstruction. Strong CBV-weighted activation was seen in the primary sensory cortex (SI) in all five rats. Functional responses were sometimes detected in the thalamus (1/5 rats) and cerebellum (2/5 rats). Typical results are shown in Figure 1. Average percent changes during stimulation were approximately 20% in SI, 7% in thalamus, and 8% in cerebellum. A representative time course from one rat is shown in Figure 2.

Discussion

Functional MR imaging in rodents has long focused on single-slice and multi-slice techniques. Studies of more complex brain processes that involve activation of multiple brain regions, however, require whole-brain coverage, making it difficult to achieve the desired spatial resolution without sacrificing temporal sampling or exceeding the capabilities of the hardware. The gradient-echo EPI sequence used in this study allows rapid acquisition of a 3D matrix, while the half-Fourier acquisition minimizes the acquisition time, reducing signal loss and spatial distortions at high field strengths, and thus providing optimal contrast during activation.

The percent changes observed during stimulation in this study were greater than the typical BOLD and CBV percent changes seen in spin-echo EPI functional images used in previous whole-brain work at 11.7 T (3). Spin-echo EPI refocuses some of the susceptibility changes caused by the iron oxide, but more importantly, the shortest echo time used in those studies was 20 ms. At an echo time of 20 ms, the BOLD effect has a significant and opposite effect on the image signal during activation, reducing the CBV contrast. This 3D sequence provides optimal sensitivity to CBV and improved spatial resolution, increasing the likelihood of detecting activation in small regions of the brain.

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References: 1. Silva AC, et al. J Cereb Blood Metab 1999;19:871-9. 2. Mandeville JB, et al. MRM 1998;39:615-24. 3. Keilholz SD, et al. Proc ISMRM 2003.

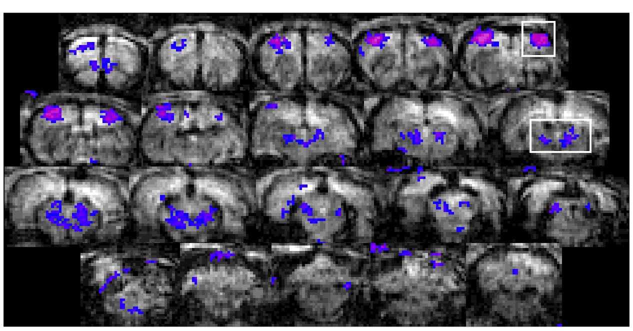

Figure 1. Typical 3D functional maps obtained during forepaw stimulation. Activation in SI and the thalamus is visible.

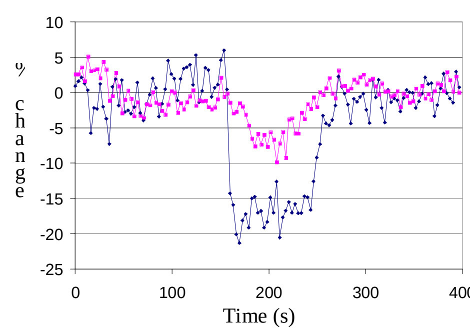

Figure 2. Time course from activated areas shown in Fig. 1. The largest percent change is seen in SI, with a smaller percent change in the thalamus.