

BOLD fMRI of the mouse barrel cortex

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Introduction: Understanding and identifying the neuronal networks of the cerebral cortex, their temporal properties, their development and plasticity are the focus of many functional imaging studies both in humans and rodents (1). In the mouse, a non-invasive method to study functionally the neural network of the barrel cortex would open the possibility to investigate the neurophysiological mechanisms responsible for plasticity during development, learning and lesion in normal and transgenic animals. BOLD functional MRI studies in mice have been difficult until now (2). This difficulty is linked to the maintenance of an appropriate physiology of the mouse during the fMRI study which has been an important topic of investigation recently (2, 3). Moreover, the small structures of the mouse brain require the use of high field strength (2) at the expense of increased susceptibility artifacts in the areas of interest or the use of dedicated cryogenic RF coils (3, 4) in order to increase the signal to noise ratio (SNR). In the present work, BOLD activations in the mouse barrel cortex under isoflurane anesthesia have been detected at 9.4T and 14.1T.

Materials and Methods: C57/Bl/6 mice (n=8, 25±3g) were anesthetized with 1.5% isoflurane in O₂. Stainless steel electrodes were inserted in the whisker pad. Electrical stimulation was performed using an external stimulator (WPI, UK) and using the following stimulus parameters (Stimulus pulse width=0.5-1ms, Stimulus frequency =1-3Hz, Stimulus current intensity=1.5-2.5mA. During stimulation, anesthesia was reduced to 1 to 1.2%. Mice were positioned in a dedicated stereotactic holder equipped with ear and teeth bars. Particular attention was taken to the fixation of the mouse head to avoid motion. Body temperature was maintained at 36.5±1°C by circulating warm water around the animals. **fMRI:** Experiments were performed on an actively shielded 9.4T/31cm bore magnet (Magnex, Varian) with 12cm gradients (400mT/m in 120µs) (n=5 mice) or on a 14.1T/26cm horizontal bore magnet (Magnex, Varian) (n=3 mice). A quadrature Transmit/Receive 14mm surface coil was used. First and second order shims were adjusted using FASTMAP (5) (water linewidth of 15-18Hz at 9.4T and 20-21Hz at 14.1T). A single shot gradient echo EPI sequence (TR/TE=3000/20ms; FOV=18x18mm or 15x15mm; matrix=64x64; slice thickness = 1mm; 6 slices, BW=200-357 KHz) was used for image acquisition. The paradigm of stimulation was 1min OFF-1min ON- 1min OFF during 10 minutes. Images were analyzed with Stimulate (6) using time-course cross-correlation with a cross-correlation coefficient above 0.3.

Results: Under isoflurane anesthesia, measurement of BOLD signal changes in the mouse barrel cortex was possible only after a short period of adjustments (15-20 minutes) including acquisition of scout and anatomical T₂-weighted images and shimming and rarely repeatable more than 2 or 3 times. Unilateral BOLD responses were found in an area corresponding to the primary somatosensory barrel field cortex (S1BF) at 9.4T and 14.1T (Fig1.A and C). BOLD time courses (Fig1.B and D) were deduced from a region of interest drawn in the BOLD activated area and demonstrated an average BOLD response of 3.6±2% at 14.1T and 2.0 ± 1% at 9.4T for an activated area of 16 pixels.

Discussion: These preliminary data demonstrate that the detection of BOLD responses in the barrel cortex of mice following electrical stimulation of the whisker pad is possible at high magnetic field. However, under isoflurane, BOLD fMRI needs to be performed with ideal conditions of SNR and shimming is required to be fast. Although forepaw stimulation at 11.7T under metomidine sedation induced reproducible and robust BOLD responses in the mouse somatosensory cortex (2), image quality was still a concern. As anesthesia is likely to interfere with signal processing, studies in awake mice would be attractive in view of the fact that many electrophysiological/optical recordings have been obtained in awake animals (7).

References: (1) Mégevand P *et al.* J Neurosci. 2009 Apr 22;29(16):5326-35. (2) Adamczak JM *et al.* Neuroimage. 2010 Jun;51(2):704-12.(3) Bosshard SC *et al.* Pain. 2010. (4) Baltes C *et al.* NMR Biomed. 2009 Oct;22(8):834-42.(5) Gruetter R *et al.* MRM,29:804,1993;(6) Strupp JP, Neuroimage, 1996, 3, S607 (7) Gentet LJ *et al.* Neuron. 2010.65:422-435.

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