

11.74T fMRI of cortical and subcortical visual networks in the rat

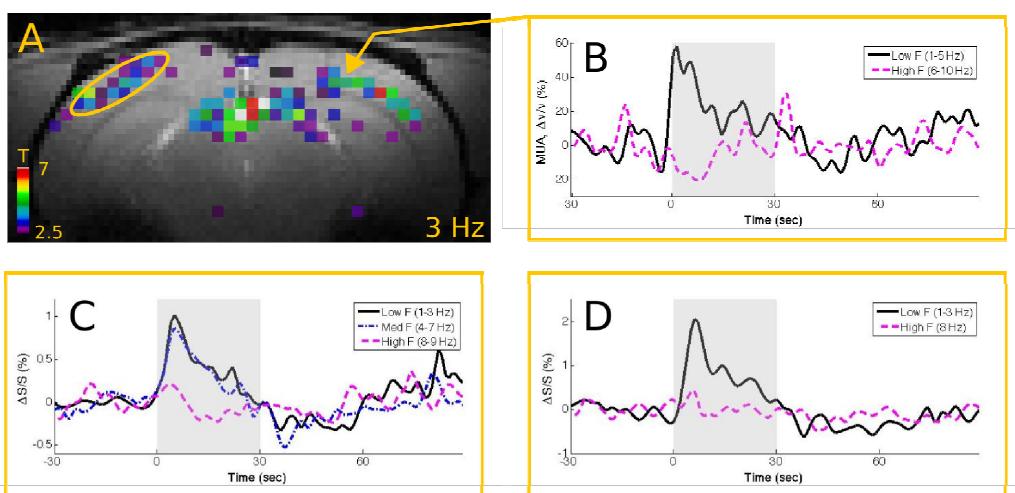
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INTRODUCTION. Though a predominantly nocturnal animal, the rat has a functional visual system, albeit of low acuity, and has at least a basic form of color vision extending into the UV range [1]. Our aim here was to develop methods to probe this system with both high field fMRI and electrophysiological techniques. Experimental setups in an imaging spectrometer are not ideally suited for studying the visual pathway of the rodent due to stringent physical constraints imposed by the imaging bore size and strong magnetic field. Here we report a method, applicable to both data acquisition scenarios, for specific and reproducible delivery of visual stimuli in fMRI as well as neurophysiology environments.

METHODS. **Stimulus delivery:** Fibre optic cables (\varnothing : 1mm) were used to guide the light of two strong LEDs, placed outside the scanner room, into the eyes of the animal as it lay positioned in the imaging bore. Acrylic lenses were used to shape the beam of light exiting the cables, to facilitate accurate and reproducible placement. The intensities of the LEDs were controlled independently using Spike 2 software and a μ 1401 DAC (CED, Cambridge, UK) to adjust the voltage at the input of constant current drivers. **fMRI:** fMRI was performed on a modified 11.74T Bruker horizontal-bore spectrometer (Billerica, MA) using a ^1H resonator/surface coil RF probe. Functional images were acquired with gradient echo EPI (TR/TE=1000/12.53 ms). **Electrophysiology:** The rat was placed in a stereotaxic holder (Kopf Instruments, Tujunga, CA) on a vibration-free table inside a Faraday cage. Burr holes above the primary visual region [4 mm lateral, 6.0 mm posterior to bregma] were drilled and tungsten microelectrodes (FHC, Bowdoinham, ME) inserted to a depth of layer 4 (~900 μm). **Animal preparation:** Long-Evans "hooded" rats were tracheotomized under isoflurane (2.5%), artificially ventilated (70% N_2O , 30% O_2) and maintained under α -chloralose anesthesia (40 mg/kg/h, i.p.). Vaseline was applied liberally to the eyes to prevent drying during the experiments.

RESULTS. Light stimuli were delivered bilaterally for 30 s (shaded areas in the plots) with a 50 ms pulse width. A coronal slice at ~7 mm posterior to bregma (A) exhibited BOLD responses during a single trial of 3 Hz stimulation of white light (25 lux) where activations were observed bilaterally both in visual cortices and superior colliculus. We recorded ensemble neuronal activity from the right visual cortex in response to flashing green light at different frequencies (B). A robust (>40%) mean spike rate increase was observed for low (1-5 Hz) but not high (6-10 Hz) frequency stimuli. Wavelet-denoised BOLD time courses extracted from the ROI circled in (A) are shown in (C) where the BOLD responses agree with the MUA data shown in (B). These localized BOLD responses were reproducible in another subject (D), in which responses were observed for low (1-3 Hz) but not high (8 Hz) frequency stimuli.



DISCUSSION. We have shown that our method of stimulus delivery elicits brain responses in cortical and subcortical structures of the rat visual pathways detectable with fMRI. The delivery method allows identical stimuli to be presented on the neurophysiology bench, thereby offering insights into the neuronal causes of the observed BOLD signal changes. These preliminary results extend the previous observation of frequency-dependence of BOLD responses to full-field stimuli with fMRI [2] and add to the growing body of BOLD and LDF data in the rat visual domain [3]. We conclude that the disadvantageous conditions for stimulus presentation during fMRI are partly offset by the ability to track hemodynamic and electrophysiological signal changes in networks consisting of both superficial and deep regions of the brain.

REFERENCES. [1] Jacobs *et al.* (2001). *J Exp Biol.* 204:2439-46. [2] Van Camp *et al.* (2006). *J Neurophysiol.* 95(5):3164-70. [3] Schulte *et al.* #3214, *Proc 15th ISMRM*, Berlin, Germany, 2007.

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