MAPPING THE VISUAL PATHWAY IN THE MOUSE BRAIN USING SNAPSHOT FMRI

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Target Audience: Researchers in the fields of preclinical imaging, mouse brain fMRI, and transgenic mouse models.

Purpose: To demonstrate the use of visual stimulation as a viable task for mouse brain fMRI, and to assess the use of snapshot GE-EPI as a way of reducing image distortion.

Introduction: Mouse brain functional magnetic resonance imaging (fMRI) is significantly challenging, yet it is an increasingly active field of neuroscience, with efforts being made to characterise both task-based [1] and resting state networks [2, 3]. High-field mouse brain fMRI is technically demanding due to the requirement for small voxels, the difficulty of physiological monitoring, and image distortion due to $\mathbf{B_0}$ inhomogeneities. The visual pathway represents an important research target for mapping in clinical and basic science applications. Previous task-based studies in the mouse have focused on electrical stimulation of the fore/hind paw[4, 5]. However, visual stimulation in the mouse has been relatively unexplored [6], with the only existing data reporting highly atypical BOLD responses when compared to rats and humans [7, 8]. In this work, we aimed to characterise the BOLD response to visual stimulation in the mouse brain. Furthermore, we also explored the possible benefits of snapshot GE-EPI [9] to reduce image distortion, balanced against an accompanying SNR penalty. This represents the first application of snapshot EPI to mouse brain task-based fMRI.

Methods: Female C57BL6/J mice ((19.0 ± 0.3) g, n = 4) were used in this study. Anaesthesia induction and animal preparation was conducted under 2% isoflurane. Medetomidine (0.4 mg/kg for an initial bolus, 0.8 mg/kg/hr for constant infusion, subcutaneous injection to the flank [4]) was used during data acquisition. This protocol produced a stable respiration rate of (170 ± 20) breaths per minute. Animals were continuously maintained on a gas mixture of 0.1 L/min of O_2 and 0.4 L/min of medical air, and kept at (37.5 ± 0.4) °C. Because the eyes were open for the duration of the experiment, eye cream (Lucrilube) was used to prevent drying of the cornea.

A 9.4T VNMRS horizontal bore MRI scanner (Agilent Inc., Palo Alto, CA) was used with a 72 mm inner diameter volume coil for RF transmission (Rapid Biomedical), and the signal was received using a 2 channel array head surface coil (Rapid Biomedical). fMRI data were acquired using GE-EPI with 1-4 snapshots (compressed segments) (FOV = 35 x 35 mm^2, matrix size = 96 x 96, 12 axial slices each 0.5 mm thick, slice gap 0.1 mm, TR = 2.5 s, TE = 19 ms, total scan time 3.5 minutes).

For visual stimulation, a fibre optic cable was placed in between the mouse head and the surface coil. The stimulus consisted of 445 nm light from a laser (Omicron) passed through the cable, and scattered off the inside of the surface coil. The fMRI paradigm consisted of 40 seconds of rest followed by 20 seconds of visual stimulation (10 Hz, 10 ms pulse duration, 0.3 mW (time averaged)), repeated three times per scan. Acquisition of fMRI data was conducted twice at each number of snapshots in an interleaved, pseudorandom manner. Data processing and analysis was completed using the standard SPM8 (www.fil.ion.ucl.ac.uk/spm/software/spm8/) fMRI pipeline. Statistical parametric maps were generated using one tailed t-tests and FWER thresholded at p = 0.05.

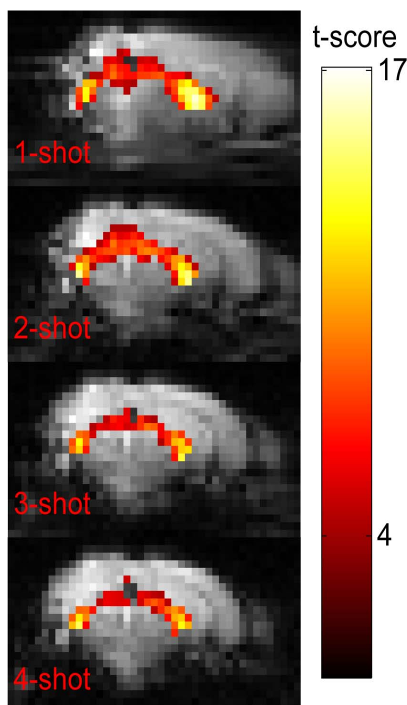

Figure 1. BOLD activation maps of the response to visual stimulation in the same slice of a single subject, demonstrating the effect of the number of snapshots on spatial and temporal signal quality.

Results: fMRI activation maps overlaid on EPI images are shown in Fig. 1. Visual inspection suggests that as the number of shots used in the GE-EPI increases, the distortion due to $\mathbf{B_0}$ inhomogeneities is reduced, but the number of voxels that pass the activation threshold fall. Activation in the lateral geniculate nuclei and the superior colliculus was detected in all subjects.

Conclusion: In this study we demonstrate a robust fMRI response to visual stimulation in the mouse brain using a free breathing, recoverable protocol with medetomidine anaesthesia. Unlike the previous study [6], we report a BOLD response that is tightly coupled to light stimulus in brain regions concordant within existing rat brain studies [7]. We have demonstrated that BOLD signals can be detected with 4 shots, providing a marked reduction in image distortion with no loss of temporal resolution. This is the first study to map the functional response to a visual stimulus in the mouse brain using snapshot GE-EPI.

References:

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