Functional MRI of the visual pathway in conscious, awake marmosets

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Purpose: The common marmoset (*Callithrix jacchus*), a small New World monkey with a highly developed visual cortex, is an emerging model to study primate visual processing. Marmosets have accessible visual areas on lissencephalic cortex, they hold promise for genetic manipulation, and they are easy to breed. Here we demonstrate a methodological approache to measure robust BOLD fMRI signals in response to visual stimuli in awake, behaving animals.

Method: Conscious awake marmosets, were acclimated to lying in the sphinx position inside a 7T horizontal bore scanner and trained to maintain their gaze at an LCD screen showing different categories of visual stimuli. A custom-printed helmet restricted each subject's head movement; likewise, a cylindrical cradle restrained the body (**Figure 1**). Training consisted of a step-wise procedure requiring several weeks, during which time the animals learned to maintain their gaze within a 5-degree window corresponding to the size of the visual stimuli. Eye position was monitored using a video-based eye tracking system and required calibration where the animal made a saccade to one of four eccentric stimuli. Subjects were taught to look at a sequence of images within a category in a block design paradigm, in which images were shown every 0.5 seconds for 16 seconds and a liquid reward was given every 1.5 seconds if the gaze was maintained. During the task performance, echo-planar imaging scans were collected to monitor category-selective blood oxygen level dependent (BOLD) responses throughout the marmoset brain. Eighteen axial slices of high-resolution (0.5 x 0.5 x 1 mm voxel size) functional scans were facilitated by an 8-channel receive surface coil embedded within the helmet[1], affording full brain coverage with a high signal-to-noise ratio.

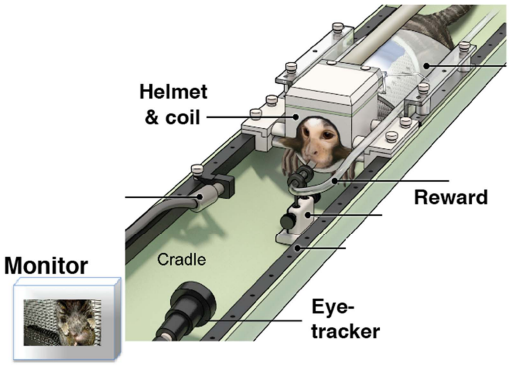

Figure 1. Setup of awake visual fMRI of marmoset

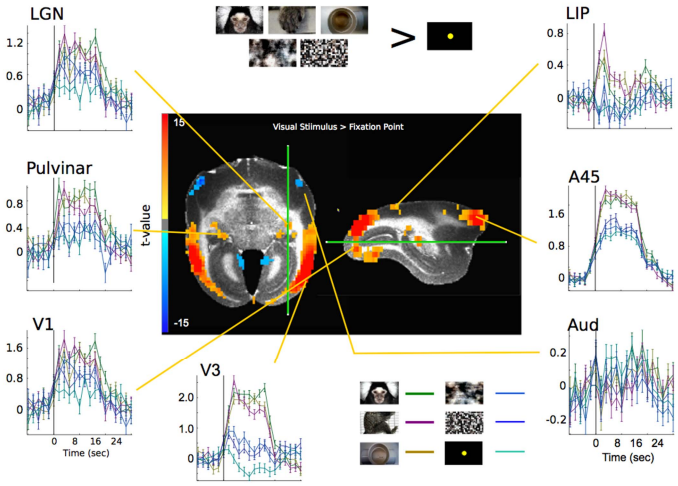

Figure 2. Visual responses to various stimuli in cortical and subcortical areas

Results: Robust BOLD fMRI responses to various complex visual stimuli, including faces, bodies, and common objects were obtained. Contrasting these stimuli to the fixation point condition produced clear visual-evoked activities in cortical (e.g. V1, V3, LIP, A45) and subcortical (e.g. LGN, pulvinar) areas[2] (**Figure 2**, with the corresponding BOLD signal time courses throughout the block of the representative voxel in the area). The responses in ventral pathway (e.g. V3, V4, TEO, TE), pulvinar, and prefrontal cortex (e.g. A45) were stronger to structured stimuli than to scrambled controls (**Figure 3**, and also see the time courses in **Figure 2**)

Conclusion: We established that we can reliably activate marmosets' brain with complex natural visual stimuli and record BOLD signals in conscious, awake animals. These findings demonstrate the promise of the awake, behaving marmoset as a model for studying primate vision using fMRI. Simultaneous electrophysiological recording, optogenetic interventions combined with fMRI are potential future directions.

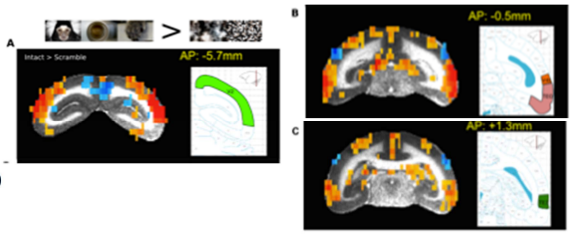

Figure 3. Structured stimuli elicit higher response compared with scrambled controls

Reference: 1. D. Papoti et al., A whole-brain 8-channel receive-only embedded array for MRI and fMRI of conscious awake marmosets at 7T. *ISMRM* (2013
2. G. Paxinos et al., The Marmoset Brain in Stereotaxic Coordinates. (2012)