

INVESTIGATION OF BOLD RESPONSE IN SOMATOSENSORY PATHWAY OF AWAKE MARMOSETS USING HIGH RESOLUTION FMRI

Cecil Chern-Chyi Yen¹, Daniel Papoti¹, and Afonso C. Silva¹

¹CMU/LFMI/NINDS, National Institutes of Health, Bethesda, MD, United States

Target Audience:

Researchers in the field of biophysics, translational science, neuroscience, and psychology

Purpose:

Since the discovery of blood oxygenation level dependent (BOLD) contrast in 1990(1), BOLD fMRI has become the primary neuroimaging modality to investigate human brain function. To better interpret the result from the BOLD fMRI, a comprehensive understanding of the spatiotemporal characteristic of the BOLD response is critical. However, higher spatiotemporal MR signal acquisition demands higher magnetic field and gradient strengths, and optimal coil design. In previous proceedings (2,3), we have demonstrated the use of conscious, awake marmosets as a surrogate model to study the somatosensory pathway. Marmosets are small non-human primates, which are phylogenetic closer to human and share many similarities in cerebral vasculature (4). Besides, marmosets can be trained to behave inside the magnet so as to avoid the confounds of anaesthesia on both the neural and hemodynamic responses. Here, we report our high-resolution fMRI results in behaving marmosets using a novel RF coil design and refined data processing scheme.

Methods:

Two adult marmosets were acclimated to body and head restraint inside a horizontal 7T/30cm MRI spectrometer (Bruker-Biospin Corp., Billerica, USA) equipped with a 15cm gradient coil (Resonance Research Inc., Billerica, USA). The animals' heads were comfortably immobilized by custom-built helmets shaped to each individual's head anatomy. Vital signals, including respiratory chest movement and oxygen saturation, were constantly monitored by a polygraph recording system (BIOPAC System Inc, Goleta, USA). Two 4-element coil arrays (15.5 mm inner diameter per coil) tailored to individual helmet were used to receive the MR signal(5). BOLD functional images were obtained using a 2D gradient-recalled echo planar imaging (EPI) sequence from eight coronal slices (TE/ TR= 26.8/ 1000ms; FOV/ thickness= 32x20/ 1mm; matrix= 128x80). T₂-weighted anatomical images were obtained using a 2D rapid acquisition with relaxation enhancement sequence from the same slices as EPI (TE/TR= 72/6000ms; FOV/thickness= 32x20/1mm; matrix= 256x160). Median and ulnar nerves were noninvasively stimulated (pulse frequency= 50Hz, intensity= 2mA, duration= 0.4ms) by pairs of electrode pads placed across both wrists. The bilateral stimulus paradigm of one epoch was 20s off, 20s on and 20s off. Slice time correction, motion correction, and co-registration with T₂-weighted anatomy were applied on BOLD functional images using AFNI(6). All epochs except those with movement larger than half of the pixel in any of the three axes as accessed by AFNI were then averaged together. Furthermore, BOLD activation maps were calculated and region of interests were determined by empirical thresholding and clustering in AFNI.

Results:

As shown in Fig 1, robust BOLD responses were detected in the primary (S1) and secondary somatosensory (S2) areas, as well as in the caudate nucleus (Cd). In Fig 2, BOLD percent change time course of S1 and S2 were averaged over four sessions of the two marmosets. BOLD response in both areas exhibit biphasic responses with a fast response peaks around 6s whereas a slow response sustains until the end of the stimuli, which corroborate with the results reported previously (2). Comparing between S1 and S2, BOLD response seems higher in S2 in both peak and sustain response.

Discussion and Conclusion:

In the present study, we have demonstrated the potential of a novel platform to study the spatiotemporal characteristic of the BOLD response using awake marmoset. By using the phase-array-embedded helmet, it is possible to minimize the head motion while achieving high SNR in the cortical surface. In addition, AFNI's motion correction and co-registration algorithm effectively reduces the small head motion and improves the statistical power. By using a strict discarding criterion for the head movement resulting in about 50% of acceptance rate, the motion artifact is significantly minimized after extensive averaging of 20 or more motionless epochs. Although not yet implemented in the current study, physiological artifact, like respiration and pulsation, can also be removed by constructing a regressor from the physiological recording using AFNI. In the future, group averaging across multiple animals can be achieved by co-registered the functional data to a high resolution T₂-weighted template and the atlas(7).

References:

1. Ogawa S, Lee TM, Kay AR, Tank DW. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proceedings of the National Academy of Sciences of the United States of America* 1990;87(24):9868-9872.
2. Liu JV, Huberty M, Silva AC. Ipsilateral fMRI Response in Primary Somatosensory Cortex (Area 3b) of Awake Marmosets. 2011; Montreal. ISMRM.
3. Hirano Y, Liu J, Silva AC. Facilitation of the BOLD Response to Bilateral Somatosensory Stimulation in Awake Marmosets. 2011; Montreal. ISMRM.
4. Silva AC, Liu JV, Hirano Y, Leoni RF, Merkle H, Mackel JB, Zhang XF, Nascimento GC, Stefanovic B. Longitudinal functional magnetic resonance imaging in animal models. *Methods in molecular biology* 2011;711:281-302.
5. Papoti D, Yen CC, Mackel J, Merkle H, Silva AC. An embedded 4-channel receive-only array for fMRI of the somatosensory pathway in conscious awake marmosets at 7T. 2012; Lisbon. ESMRMB.
6. Cox RW. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and biomedical research, an international journal* 1996;29(3):162-173.
7. Newman JD, Kenkel WM, Aronoff EC, Bock NA, Zametkin MR, Silva AC. A combined histological and MRI brain atlas of the common marmoset monkey, *Callithrix jacchus*. *Brain research reviews* 2009;62(1):1-18.

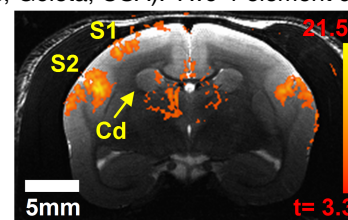


Fig. 1. BOLD functional map overlaid on corresponding T₂-weighted anatomy in one representative marmoset.

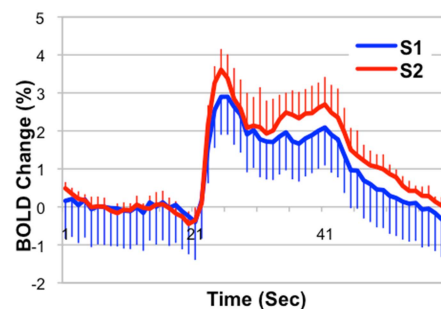


Fig. 2. Averaged BOLD percent change time courses over four sessions. Error Bar= Standard Deviation