Neuronal Current MRI in the Octopus Visual System

Xia Jiang[1], Hanbing Lu[2], Shuichi Shigeno[3], Li-Hai Tan[4], Yihong Yang[2], Clifton W Ragsdale[3], and Jia-Hong Gao[1]

[1]Brain Research Imaging Center and Department of Radiology, University of Chicago, Chicago, IL, United States, [2]Neuroimaging Research Branch, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD, United States, [3]Department of Neurobiology, University of Chicago, Chicago, IL, United States, [4]State Key Lab for Brain Research, University of Hong Kong, Hong Kong, China

Purpose

Much effort has been devoted to the development of neuronal current MRI (nc-MRI), where the small magnetic field change caused by electric currents during neuronal activation is used to map brain function. Since the neuronal current is a direct reflection of neural activity, nc-MRI should offer spatial and temporal resolutions superior to those of traditional functional MRI (fMRI) methods, such as the blood oxygen level dependent (BOLD) mechanism, where the signal response is delayed in time and spread out in space due to the hemodynamic response function. However, the feasibility of the nc-MRI technique has been subject to intense debate, with contradictory results reported by different groups (1-2).A major confounding factor in these studies is the residual BOLD signal. To address this problem, tissue preparations free from blood have been employed to study nc-MRI; however these approaches required electrical or drug stimulation and are not applicable to sensory-related stimulation. In this study, we tested the feasibility of naturally evoked nc-MRI in the octopus visual system. Octopus blood uses copper based hemocyanin for oxygen transport, which is free from a BOLD effect (3). Hence, this unique animal model allowed us to carry out *in vivo* study of nc-MRI without a BOLD confound.

Material and Methods

Electrophysiology and nc-MRI measurements were performed in the retina and optic lobe (OL) of *Octopus bimaculoides*. The animals were anesthetized with a 1.5% ethyl alcohol solution. To characterize the electric activity in the octopus visual system, we used the electroretinogram (ERG), where the response in the retina is measured with surface electrodes, and recorded the local field potentials (LFP) in the OL using metal electrodes inserted into the OL. These measurements were made for different light stimulation durations and inter-stimulus intervals (ISI) to determine the optimal stimulation paradigm, and they were done before and after nc-MRI scans to ensure tissue viability. nc-MRI scans were carried out on a Bruker 9.4T scanner with a single shot gradient echo EPI sequence and the following parameters: FOV = 2x2 cm^2, matrix size = 64x64, slice thickness = 1 mm, TR/TE = 1 s/18 ms and flip angle = 70°. Two slices were used to cover the retina and the OL, respectively, and the acquisition times were matched to the peak electric activity determined by ERG and OL LFP. A light stimulation duration of 50 ms and an ISI of 2 s allowed for stimulation every other TR. Each scan lasted for 2 hours, accumulating 7200 data points. A two-sample t-test was used to compare the signal from even and odd numbers of TR for both signal magnitude and phase.

Results

Electrophysiological recording found consistent and robust responses from both the retina and OL in six octopuses (Fig. 1), with the ERG peaking earlier than the OL LFP. nc-MRI scans in eight octopuses found only randomly scattered "activated" voxels at $P < 0.01$ level (Fig. 2). After correction for multiple comparisons, no statistically significant activation was found in either retina or OL.

Discussion and Conclusion

In this study we employed a novel animal model that, for the first time, allowed *in vivo* study of nc-MRI without a BOLD confound. Based on power analysis and the temporal SNR of the MRI time series, we estimated that the detection threshold in our experiment was better than 0.2%/0.2° for magnitude and phase changes respectively. The failure to detect any statistically significant changes at such levels suggest that sensory evoked neuronal currents are too weak to be detected with conventional MRI technique. Other types of activities, such as alpha waves or epileptic seizures, or more sensitive detection techniques, such as superconducting quantum interference devices, might be more promising directions for future studies.

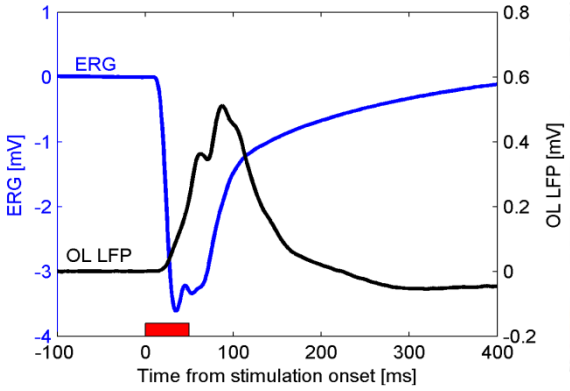

Figure 1. Electrophysiological recordings in the octopus visual system in response to 50 ms light stimulation (indicated by the red box).

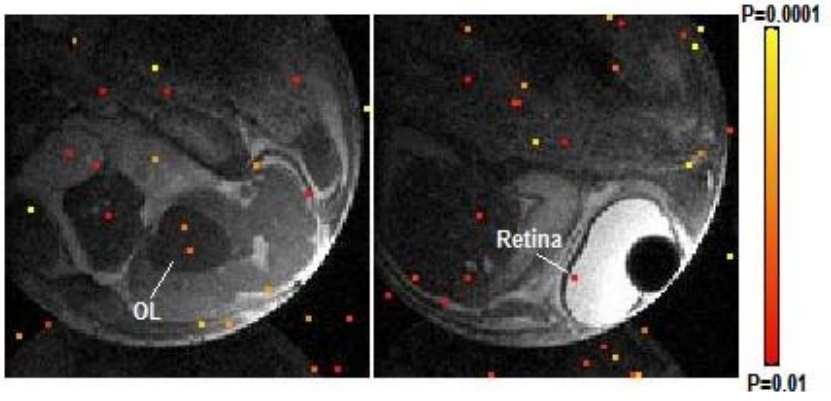

Figure 2. P-static map for phase changes for two nc-MRI slices, overlaid on corresponding RARE anatomical images. The P-maps were thresholded at $P < 0.01$ level (uncorrected).

References. [1] Xiong J, Fox PT, Gao J-H (2003) Directly mapping magnetic field effects of neuronal activity by magnetic resonance imaging. Hum Brain Mapp 20:41–49. [2] Chu R, de Zwart JA, van Gelderen P, Fukunaga M, Kellman P, Holroyd T, Duyn JH (2004) Hunting for neuronal currents: absence of rapid MRI signal changes during visual-evoked response. NeuroImage 23:1059–1067. [3] Rawlinson WA (1941) The effect of oxidizing agents on haemocyanin. Aust J Exp Biol Med Sci 19:137–141.