Session 092 - Optogenetic Approaches to Studying Neural Circuit Function

Add To Itinerary

92.15 / KKK13 - Stable, chronic two-photon imaging in awake, behaving rhesus macaque.

November 12, 2016, 1:00 - 5:00 PM | Halls B-H

Presenter at Poster
Sat, Nov. 12, 2016, 3:00 PM - 4:00 PM

Session Type
Poster

Authors
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Disclosures
X. Sun: None. **E. Trautmann:** None. **D. O'Shea:** None. **S. Ryu:** None. **J. Marshel:** None. **W. Allen:** None. **I. Kauvar:** None. **C. Ramakrishnan:** None. **K. Deisseroth:** None. **K. Shenoy:** None.

Abstract
Optical functional imaging, such as 2-photon (2P) calcium imaging, have become powerful tools for investigating functions of neural circuits *in vivo*. Translating these techniques to non-human primates enables recording hundreds or thousands of neurons simultaneously with single-neuron resolution, tracking the same neurons across multiple sessions, combining functional recordings with high resolution structural imaging, and identifying cell types using genetic labeling. We have developed a platform for performing 2P imaging in awake, behaving rhesus monkeys and have demonstrated: 1) dense expression of GCaMP across PMd, M1, and S1, 2) stable imaging of neurons during a motor behavioral task, 3) imaging neurons 500 microns below the surface in highly-scattering primate cortex, and 4) tracking the same neurons across multiple days and sessions. While encouraging, the vast majority of the thousands of neurons imaged via 2P exhibited bright, filled processes and somas and did not modulate in intensity, consistent with reports of GCaMP overexpression in rodent imaging (e.g. Harvey et al., 2012). We achieved these imaging goals by addressing experimental and engineering translation challenges unique to monkey research. To screen for GCaMP constructs that express in primates, we injected 8 viral constructs at 32 sites in PMd, M1 and S1. To align with long-term monkey research timescales, the imaging chamber must maintain clarity for several months to years. We developed an imaging chamber that incorporates a transparent replaceable silicone window, which is sealed from the external environment to minimize risks of infection and opacification. Another challenge to stable imaging are the brain pulsations induced by cardiac and respiratory rhythms. To restrict brain motion, we developed a stabilization system that uses gentle pressure to restrict total XY motion to 5-10 μm for prolonged experiments. To prevent the experimental task itself from generating movement of the brain while imaging, we developed a novel rigid three-point head restraint system. Finally, to maximize the imaging depth, we used a dichroic and light guide at the back aperture of the imaging objective to collect scattered photons and maximize the photon collection efficiency. Our results demonstrate the feasibility of two-photon imaging that can facilitate a new class of systems neuroscience experiments in behaving monkeys, complementary to electrophysiological studies.