Print this Page

NEUROSCIENCE 2011

Presentation Abstract

Program#/Poster#: 306.11/YY22

Presentation Title: Optogenetic control of excitatory neurons via a red-shifted opsin in primate premotor cortex

Location: Hall A-C

Presentation time: Sunday, Nov 13, 2011, 3:00 PM - 4:00 PM

Authors: ***D. J. O'SHEA**[1], W. GOO[2], I. DIESTER[1], P. KALANITHI[3], O. YIZHAR[2], C. RAMAKRISHNAN[2], K. DEISSEROTH[2], K. SHENOY[4];
[2]Bioengineering, [3]Neurosurg., [4]Electrical Engin., [1]Stanford Univ., Stanford, CA

Abstract: Precise, targeted perturbation of neuronal activity in motor cortices would help to elucidate the mechanisms by which movements are prepared and executed. While electrical microstimulation delivered to dorsal premotor cortex (PMd) has been previously shown to disrupt this preparatory process, the difficulty of targeting and concurrently observing the effects of electrical stimulation in neural circuits precludes more informative perturbation experiments. Optogenetics is a complementary approach that allows temporally precise control of genetically-defined neural populations. We therefore sought to expand the optogenetic toolkit for perturbation of neural activity in behaving primates. We have previously reported functionality of excitatory (ChR2, SFO) and inhibitory (eNpHR2.0) opsins in rhesus macaque cortex under pan-neuronal human promoters (hThy1, hSyn) and using AAV5 as the delivery vector, motivated by the translational advantages of AAV vectors which derive from their clinical safety (Diester et al., 2011). To increase the volume of tissue addressed by optogenetic perturbation, we here exploit the reduced attenuation of red light in brain tissue. We selected the potent red-shifted opsin C1V1 (Fenno et al., SfN 2010), which has not previously been used in primates. To achieve cell-type specificity, we employed the previously validated CaMKIIα promoter to target opsin genes to excitatory neurons (Zhang et al., 2007; Aravanis et al., 2007; Han et al., 2009; Lee et al., 2010). Here we report functionality of AAV5-CaMKIIα-C1V1 in macaque cortex. Light pulses of 2-ms at 473 nm (blue), 561 nm (green), and 635 nm (red) reliably

drove spiking in presumed pyramidal neurons. Low light levels (12 to 286 mW/mm2 through a 200 μm optical fiber with 0.48 NA) were sufficient to drive spiking responses. We assess neural modulation both with single-unit data and local field potentials. Combining the advantages of AAV delivery, cell-type specificity, and long wavelength activation helps expand the collection of primate-optimized optogenetic tools for systems neuroscience.

Disclosures: **D.J. O'Shea:** None. **W. Goo:** None. **I. Diester:** None. **P. Kalanithi:** None. **O. Yizhar:** None. **C. Ramakrishnan:** None. **K. Deisseroth:** None. **K. Shenoy:** None.

Keyword(s): Optogenetics

MOTOR CORTEX

PRIMATE

Support: Howard Hughes Medical Institute

Michael J Fox Foundation

DARPA (REPAIR)

NIH (Director's Pioneer Award)

[Authors]. [Abstract Title]. Program No. XXX.XX. 2011 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, 2011. Online.