This Week in The Journal

Advances in All-Optical Electrophysiology

Shan Lou, Yoav Adam, Eli N. Weinstein, Erika Williams, Katherine Williams, et al.

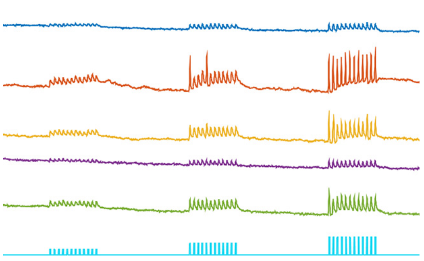
(see pages 11059–11073)

Since the demonstration that channelrhodopsins can be used to optically induce neuronal spiking, much effort has gone toward optimizing tools for all-optical electrophysiology. To achieve this goal, actuators and reporters of neuronal activity must act quickly enough to elicit and report individual spikes in trains and be sensitive enough to permit activation and recording with limited phototoxicity. Furthermore, there must be minimal spectral overlap between the actuator and reporter, so they can be combined in the same tissue without crosstalk. These criteria were previously met through mutagenesis of archaerhodopsins and channelrhodopsins, which produced the voltage indicator QuasAr2 and actuator CheRiff, respectively. When a vector (called Optopatch2) containing both constructs was transfected into cultured neurons, researchers could stimulate spikes in single cells and detect EPSPs in adjacent cells (Hochbaum et al. 2014 Nat Methods, 11:825).

Lou et al. have now created transgenic mice in which the Optopatch2 construct is flanked by LoxP sites, allowing Cre-dependent expression in specific populations of CNS and PNS neurons. Floxopatch expression had no apparent effect on mouse survival or neuronal resting electrophysiology. In dissociated cultures of PNS neurons, voltage responses measured optically were similar to those measured electrically. Moreover, individual spikes could be detected, and the overall spike width and afterhyperpolarization shape could be determined. Importantly, transgenic expression produced more uniform construct expression than electroporation, and thus the effects of optical stimulation was less variable across neurons obtained from transgenic animals.

Most notably, optically induced spiking could be recorded *in vivo*, by positioning the nodose ganglion between two coverslips. Although the signal-to-noise ratio for QuasAr2 was insufficient to detect spiking in the CNS *in vivo*, action potentials could be detected optically in acute brain slices. Resolving action potentials evoked optically in dentate granule cells required image segmentation procedures, because multiple overlapping cells were usually present in a field. Nonetheless, individual spikes could be detected, and subpopulations of neurons could be defined based on different firing properties.

These results demonstrate that *in vivo* all-optical electrophysiology is now possible in peripheral ganglia. The authors suggest that by inserting the transgene in a different location, the signal-to-noise ratio of the voltage indicator might be increased sufficiently to allow use in the CNS.



Optical stimulation (bottom trace) produced voltage responses (top 5 traces) measured optically in 5 cultured PNS neurons from a Floxopatch mouse. See Lou et al. for details.

A Rubber Appendage Illusion for Mice

Makoto Wada, Kouji Takano, Hiroki Ora, Masakazu Ide, and Kenji Kansaku

(see pages 11133–11137)

People easily recognize their own limbs when they see them. Nonetheless, most people can be made to feel that a rubber hand is their own under certain conditions. Specifically, if a person's own hand is hidden and a rubber hand is placed in their visual field, when an experimenter strokes the rubber and real hands simultaneously, the subject soon begins to perceive the rubber hand as theirs. Not only do they report a feeling of ownership of the hand, but their perception of their real hand's positions shifts towards that of the rubber hand. Moreover, they show anxiety responses when the rubber hand is threatened. Importantly, this illusion only develops if stroking of the real and artificial hands is synchronous: asynchronous stroking disrupts the illusion. The illusion is thought to depend on activity of neurons in the premotor and posterior parietal cortex that respond to both visual and tactile information (Ramakonar et al. 2011 J Clin Neurosci 18:1596).

Although some evidence suggests that the rubber hand illusion can be generated in monkeys, whether non-primates can experience this illusion has been unclear. Wada et al. now provide evidence that a rubber tail illusion can be induced in mice. The procedure shared many features of the rubber hand illusion: an artificial tail was presented in an anatomically plausible position while the animal's own tail was hidden. After the artificial and real tails were stroked synchronously or asynchronously, the experimenter firmly grasped the rubber tail. Mice were more likely to respond with a head movement in the synchronous stroking condition than after asynchronous stroking. Furthermore, when two rubber tails were in view and only one of them was stroked synchronously with the real tail, mice were more likely to respond when the stroked tail was grasped than when the unstroked tail was grasped.

These results suggest that synchronous stroking of a visible rubber tail and a mouse's real tail causes the mouse to respond to the rubber tail as if it were its own. This suggests that mice experience body ownership, a basic form of self-awareness. The development of this procedure opens the door for exciting research on the neural mechanisms underlying body ownership.

This Week in The Journal was written by Teresa Esch, Ph.D.