This Week in The Journal

Species Differences in Neurons Controlling Frog Calls

Charlotte L. Barkan, Darcy B. Kelley, and Erik Zornik

(see pages 5325–5337)

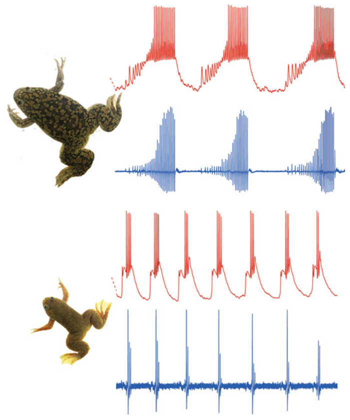
Speciation is often accompanied by divergence of courtship behaviors, which reduces interbreeding between emerging species. Divergence of calls used to attract mates (advertisement calls) is particularly common. Although some birds learn songs from tutors, in many species courtship calls are innate. In such cases, song divergence likely involves modification of song-producing motor circuits present in a common ancestor. Investigating differences in the song circuitry of closely related species might therefore provide insight into how evolution shapes behavior.

Such reasoning led Barkan et al. to examine differences in the neural circuits controlling advertisement calls in *Xenopus* frogs. Depending on the species, these calls range from single sound pulses (clicks) to rapid trains of pulses (bursts or fast trills) that are repeated at characteristic intervals. The calls of *X. laevis* and *X. petersii* comprise fast trills, but the duration and period of these trills is longer in *X. laevis*.

Xenopus vocal patterns are generated by neurons in the hindbrain parabrachial area (PB_x) and vocal motor nucleus. Previous work in *X. laevis* identified a group of PB_x neurons that show NMDA-dependent oscillations during bouts of calling. Notably, the duration and period of these oscillations match those of fast trills. Therefore, differences in the activity of these neurons might underlie differences in call pattern (Leininger and Kelley, 2015 Cytogenet Genome Res 145:302–314).

To test this hypothesis, Barkan et al. first identified homologous PB_x neurons (named fast-trill neurons) in *X. petersii*. As predicted, the period and duration of oscillations matched those of these frogs' calls. In both species, fast-trill neurons spiked at or just before the beginning of the motor command driving each fast trill. Importantly, similar oscillatory patterns were induced by NMDA application when spiking was blocked. Moreover, current injections produced longer spike trains in *X. laevis* than in *X. petersii*.

Together, these data suggest that differences in NMDA currents or ion channels that shape oscillatory behavior in fast-trill PB_x neurons contribute to species-specific differences in vocalizations. To confirm this hypothesis, oscillatory behavior in these neurons should be experimentally manipulated. After that, identifying the responsible channels and determining how their function or regulation differs across species should help elucidate how *Xenopus* advertisement calls diverged during evolution.



The depolarization duration and period of oscillations in fast-trill neurons (red traces) matches those of motor commands that drive calls (blue traces), and both are longer in *X. laevis* (top) than in *X. petersii* (bottom). See Barkan et al. for details.

Effects of Brief Cholinergic Activation in Somatosensory Cortex

Rajan Dasgupta, Frederik Seibt, and Michael Beierlein

(see pages 5338–5350)

Attention is thought to facilitate stimulus detection by increasing responses of sensory cortical neurons to relevant sensory inputs and by decreasing ongoing synchronous activity manifest in slow oscillations. These effects are mediated largely by the actions of acetylcholine (ACh), which produces short- or long-lasting depolarization or hyperpolarization, depending on the receptor, neuron type, and cortical layer. For example, ACh depolarizes somatostatin-expressing inhibitory neurons in upper layers of visual cortex by activating nicotinic and M1-type muscarinic receptors; this suppresses slow oscillations and leads to disinhibition of excitatory neurons, which might make them more receptive to sensory input. ACh also depolarizes excitatory neurons in layers 2/3 and 5 of rodent somatosensory cortex via M1 receptors. But ACh hyperpolarizes excitatory neurons in layer 4 of somatosensory cortex by activating M2-type receptors (Muñoz and Rudy, 2014 Curr Opin Neurobiol 26:149). In many previous experiments, ACh was applied for several seconds, mimicking the slow, tonic, and diffuse increases in ACh that were long thought to drive cortical state changes *in vivo*. But recent work has shown that faster, more localized ACh transients occur during ongoing behaviors, such as whisking. Whether ACh exerts similar effects on cortical neurons over these shorter time scales has been unclear.

Dasgupta et al. addressed this question by examining the effects of brief (5 ms) activation of channelrhodopsin-expressing cholinergic fibers in mouse somatosensory cortical slices. Cholinergic stimulation suppressed long-latency recurrent activity evoked by extracellular stimulation in layer 4 excitatory neurons, and thus reduced spiking. The suppression persisted for at least 5 s. Although stimulation of cholinergic fibers led to transient activation of nicotinic AChRs on inhibitory neurons in upper cortical layers, persistent suppression required activation of muscarinic AChRs in layer 4. In this layer, most fast-spiking interneurons and excitatory neurons exhibited muscarinic IPSCs resulting from activation of G-protein-coupled inwardly-rectifying potassium channels.

These results show that even local, transient release of ACh can produce long-lasting suppression of recurrent cortical activity by activating muscarinic receptors in layer 4 neurons. The suppression of recurrent activity might help to accentuate responses to sensory input from the thalamus during active whisking. Future work should examine how locally blocking specific receptor subtypes affects sensory discrimination.

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