In zebra finches, as in all songbirds, song learning and production are mediated by a discrete collection of forebrain nuclei referred to as the song system. Song is learned from an adult male tutor early in life, and crystallizes by 100 days of age. Both juvenile song learning and adult song maintenance are dependent on auditory feedback.

In urethanized birds, most song system nuclei contain many neurons that are robustly selective for the bird's own song (BOS). It has long been hypothesized that these responses exist in the nuclei that produce song as an autogenous feedback reference for guiding song behavior. However, the expression of these responses is highly dependent on the bird's behavioral state. During sleep, song system neurons burst not only in response to song, but spontaneously as well. In the motor nucleus RA, these bursts are highly temporally precise and match the motor patterns produced by that cell during singing. They therefore represent sleep replay of learned song motor patterns, and may provide a mechanism for "offline" modification of motor patterns based on feedback. In awake, freely moving birds, these bursts are essentially absent from RA except when the bird sings, and bursting and auditory responses are weaker and less prevalent in HVc, another song motor nucleus afferent to RA.

Preliminary pharmacological manipulations suggested that neuromodulatory input to the song system may mediate this gating, and that it does so at the level of HVc. Injections of norepinephrine (NE) into HVc, but not RA, led to a suppression of auditory responses in RA that was similar to that seen in the awake bird. Further tests with agents specific to adrenergic receptor subtypes, however, suggested that NE did not mediate behavioral state-dependent changes in song system activity. HVc and RA receive cholinergic input from the ventral paleostriatum (VP), a basal forebrain region similar to the mammalian nucleus basalis of Meynert (NB). Neurons in NB are known to modulate their activity according to the sleep-wake cycle, and are activated by stimuli with attentional or behavioral significance. We therefore tested the effects of the cholinergic system on RA BOS responses responses.

Injections of the cholinergic agonist carbachol into HVc strongly and consistently caused a sustained suppression of responses to BOS in urethane anesthetized zebra finches (n=6/6, $p < 0.001$). The majority of injections (4/6) also resulted in an increase in the ongoing, spontaneous discharge of RA cells ($p < 0.001$), a feature also observed in RA cells during wakefulness. Injections of muscarine produce similar results on auditory driven (n= 3/3, $p < 0.001$) and spontaneous (n=3/3, $p < 0.001$) activity. Injections of nicotine in HVc also elicit auditory suppression in RA, but only briefly and at high doses (3/7 injections, $p < 0.001$), an effect possibly due to desensitization.

We also tested the effects of stimulating the source of cholinergic input to the song system in VP. Short bursts of electrical stimulation (400 s, biphasic pulses at 25-70 A and 100-500 Hz for 100-1000 ms) caused a large, significant reduction in response to BOS (n=17/20 stimulations, $p < 0.001$) that lasted a variable length of time ranging from about 15 s to about 20 min. Additionally 17/18 SU showed a significant increase in spontaneous rate ($p < 0.01$). These effects were due to the stimulation of cell bodies in VP and not

nearby fibers, as injections of glutamate produced similar results for auditory driven ($n=4/4$, $p < 0.001$) and spontaneous activity ($n=4/4$, $p < 0.001$). Finally, the effects of VP stimulation were blocked or greatly attenuated by injections of the nicotinic antagonist DHE into HVc ($n=4/4$), but not the surrounding neostriatum ($n=2/2$). We therefore conclude that auditory input to RA can be regulated by cholinergic input to HVc that originates in VP.

The auditory regulation we demonstrate here is rapid and strong. It is consistent with a role for VP in the modulation of RA physiology according to states of sleep and wakefulness. It is also possible that VP regulates auditory feedback on a finer temporal scale during singing. Control of feedback in this manner could subserve the implementation of offline mechanisms for motor pattern modification, and by dynamically modifying response properties of different neuronal populations in HVc, might allow the duplexing of sensory and motor signals in that structure during song. We are currently investigating the effects of cholinergic stimulation on HVc circuitry *in vivo* and *in vitro*. We are also examining the effects of disrupting this possible feedback control mechanism on song behavior through VP lesions.