Published in final edited form as:

Trends Neurosci. 2018 April ; 41(4): 167–170. doi:10.1016/j.tins.2018.02.006.

The Song Remains the Same

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Abstract

Deafness causes speech deterioration, but whether this process reflects an active or passive process is unclear. Birdsong – which is a learned vocal behavior that resembles speech in its dependence on auditory feedback – also deteriorates following deafening. In their 2000 paper, Brainard and Doupe showed that following deafening, birdsong deteriorates through an active process mediated by a cortico – basal ganglia circuit.

Keywords

Vocal learning; auditory feedback; basal ganglia; birdsong

A critical developmental milestone for humans is the imitation of appropriate speech models, a process that involves extensive vocal practice and self-monitoring of vocal performance using auditory feedback. Once learned, speech remains remarkably stable unless a major sensory, motor or cognitive deficit interferes with the speech production system. Hearing loss is one of these events. When hearing is lost, speech slowly deteriorates and can even become unintelligible. What processes – passive or active – and what brain mechanisms cause vocal deterioration following hearing loss? In a pioneering study, Michael Brainard, working with his postdoctoral advisor Allison Doupe, showed that the deafening-induced deterioration of birdsong – which, like speech, relies on auditory feedback for its learning and maintenance – is actively driven by the output of a cortico – basal ganglia (BG) circuit [1]. This pivotal finding motivated a range of experiments that highlighted the evaluative and error-correcting computations performed by BG circuitry in the context of vocal learning and maintenance. Moreover, because of the close parallels between the avian and mammalian BG [2], this study provided insights into how the BG could contribute, more generally, to the production of rapid sequential behaviors in various species, including human-specific skill such as speech, musical expression, and athletic performance.

Similar to a child learning to speak, a juvenile songbird learns to sing by memorizing and then vocally copying the song of an adult tutor. Song copying depends on the juvenile being able to hear its own song, indicating that the juvenile's brain uses auditory feedback to

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evaluate its own song in reference to an internal song target [3]. In some songbird species, including the zebra finch, auditory feedback is also used in adulthood to maintain stable performance of highly precise, previously-learned songs. Specifically, deafening an adult finch causes the spectral features of its song syllables to slowly deteriorate, and also destabilizes syllable sequences, reminiscent of changes that can occur to human speech following hearing loss [4]. These parallels between birdsong and speech have motivated intense interest in understanding the neural mechanisms of song learning and maintenance. In fact, pioneering neuroanatomical studies have identified specialized circuitry in the songbird forebrain, including a song motor pathway (SMP) essential to producing learned birdsongs [3] (Figure 1). Another major component of this “song system” is an anterior forebrain pathway (AFP) that includes a specialized basal ganglia structure (Area X) and a downstream forebrain nucleus (LMAN). Notably, although LMAN projects directly to the SMP, complete lesions of LMAN made in *adult* birds have no effect on their previously learned songs [5]. In contrast, LMAN lesions made in juveniles prevent them from copying a tutor song, raising the possibility that LMAN helps to evaluate song performance in reference to the tutor model, and then dwindles to a vestigial role once this sensorimotor learning process is complete [5].

An alternative idea is that LMAN supplies similar feedback-dependent evaluative information about vocal performance in relation to internal song targets throughout life, but the role of this feedback changes over time. In juveniles, this information guides tutor song copying, and in adults, the information helps maintain stable song output. In this scenario, deafening in adults causes a large mismatch between the feedback signal (i.e., by abolishing it) and the internal vocal target, resulting in an error signal that could actively drive vocal deterioration. By contrast, in hearing adults that have completed the process of song learning, LMAN-mediated feedback carries little mismatch information, explaining why LMAN lesions *per se*, as mentioned, have no noticeable effects on previously learned songs. In strong support of this model, Brainard and Doupe found, first, that when they destroyed LMAN in an adult finch prior to deafening, its song remained unchanged not only prior to deafness-onset, as was previously known [5], but also for many months following deafening [1]. Interpreted in the context of the model outlined above, these findings show that silencing LMAN eliminates deafness-induced song deterioration. It seems, therefore, that deafening-induced vocal deterioration is an active process likely driven by a ‘free-running’ error signal, rather than resulting from a passive process, such as the slow accumulation of uncorrected motor drift caused by age-related changes to the vocal muscles or nerves. And whereas deafening and brain lesions are relatively blunt instruments by today’s standards, the prolonged delay between deafening and the onset of song deterioration allowed the authors to more confidently assign LMAN a role in song evaluation. It’s important to note that a contemporary study showed that LMAN lesions prevent slow temporal reorganization of song following vocal nerve section [6]. Nerve section however immediately affects both vocal control and sensory feedback, making the interpretation of the findings more challenging. Together with the more definitive results of Brainard and Doupe, the two studies provided compelling evidence for LMAN as carrying an instructive error signal.

Brainard and Doupe’s illuminating result spawned many noteworthy studies that sought to more precisely define the AFP’s evaluative role in vocal learning. One attractive idea was

that LMAN detects errors in vocal performance and transmits this error signal to the SMP. Despite this idea's appeal, LMAN neurons in freely behaving juvenile and adult birds showed little auditory responsiveness, but became more excited immediately before and during singing, and this singing-related activity persisted largely unchanged when auditory feedback was disrupted by noise or prevented by deafening [7, 8]. The insensitivity of LMAN neurons to auditory feedback perturbations suggest they sit downstream of the circuitry that compares singing-related feedback and the internal song model, and instead that they transmit motor-related signals that act either permissively or instructively to guide vocal learning. Indeed, inspired by models of BG-dependent reinforcement learning, an emerging idea was that LMAN's purpose may be to drive trial-by-trial variations in song performance necessary to a reinforcement learning mechanism [2]. Consistent with this view, singing-triggered microstimulation in LMAN was found to acutely modulate the spectral features of individual syllables [9], whereas reversibly inactivating LMAN in juveniles strongly reduced the otherwise marked trial-by-trial variability in their songs [10].

A crucial question is whether LMAN – in addition to contributing to vocal variability – also adaptively biases song output, as predicted for an instructive signal. This is challenging to address in juveniles because their songs are highly variable, and the learning outcome cannot be known until months later, when song copying is complete. Here, Brainard's own group made another major contribution, by establishing that the slight trial-by-trial variations in adult song could be exploited to drive vocal learning [11]. After assessing the baseline variability of the fundamental frequency (i.e., pitch) of a syllable in an adult's song, a real-time closed-loop system was used to trigger a noise burst when the target syllable pitch fell below or above a user-determined threshold. Over tens to hundreds of renditions, the target syllable's pitch moved away from the frequency region paired with noise, in a process referred to as pitch learning. Notably, when noise was discontinued, the syllable pitch gradually returned to its baseline value, revealing that the adult's brain contains a stable internal song model in addition to retaining a modest capacity for ongoing vocal learning. The low residual variability of adult song and the ability to control the direction of changes in a syllable's pitch provided a powerful system in which to test whether LMAN generates a bias signal. Indeed, a critical study found that inactivating LMAN during pitch learning caused the target syllable to immediately revert toward the baseline, indicating that LMAN transmits an adaptive bias signal in addition to contributing to song variability [12].

An ongoing goal is to determine the nature of the evaluative machinery upstream of LMAN, including Area X and the inputs it receives from the ventral tegmental area (VTA). An influential idea is that dopamine-releasing inputs from the VTA respond to singing-related auditory feedback and selectively strengthen synapses from the song motor pathway to Area X, providing the source of the bias signal that LMAN relays to the SMP (Figure 1) [2]. Indeed, important recent studies have established that 1) auditory forebrain neurons that innervate the VTA can sense perturbations in singing-related feedback [13], 2) VTA neurons that project to Area X (i.e., VTAX neurons) encode reward prediction error that depends on the history of singing-triggered noise [14], and 3) pitch-contingent optogenetic stimulation of VTAX terminals is sufficient to drive pitch learning [15]. These experiments largely involved adult birds, so a critical remaining issue is to determine whether the same circuit mechanisms guide juvenile song copying. Both juvenile song copying and adult pitch

learning are blocked by genetic ablation of VTAX neurons or blockade of D1-type dopamine receptors in Area X, hinting that a unified circuit mechanism may underlie both types of learning [15]. Thus, in retrospect, Brainard and Doupe's pioneering study helped the field develop an expanded appreciation of the role that cortico–BG circuitry plays not only in learning a skill for the first time, but also in modifying a previously learned skill in the face of altered sensory feedback. Moreover, BG circuitry is relatively well conserved in mammals and birds, and it is likely that this circuitry initially evolved to enable motor learning in response to external reinforcement by punishment or reward. Therefore, Brainard and Doupe's study also paved the way to the insight that brain circuitry that originally evolved to enable motor learning via external reinforcement may have been exploited in songbirds and humans to enable vocal learning, a process that is internally guided and does not depend on reinforcement by appetitive or aversive external cues.

Acknowledgments

The author thanks Stephen Lisberger, Jesse Goldberg, and Katherine Tschida for reading earlier versions of this manuscript. Support was provided by NIH 1R01-NS-099288 (RM) and NSF IOS-1354962 (RM).

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Figure 1. Schematic of the song system and comparative anatomy of cortico-BG circuits in songbirds and mammals

A) The songbird brain (shown in sagittal view) contains specialized song circuitry, including a song motor pathway (SMP; red), important for song production, and an anterior forebrain pathway (AFP; black), which is necessary for juvenile song copying and adult forms of auditory-dependent vocal plasticity. B) The AFP shares many similarities to cortico-BG circuitry in mammals. These include a striatopallidal structure (Area X in songbird) that is interposed between cortical premotor and thalamic regions, and that receives input from dopamine releasing neurons in the ventral tegmental area (VTA). Other abbreviations: HVC (used as a proper name); RA (robust nucleus of the arcopallium), DM (dorsomedial nucleus of the intercollicular midbrain region), nXIIts (tracheosyringeal part of the hypoglossal motor nucleus), VRG (ventral respiratory group, comprising nucleus retroambigualis (RAm) and nucleus parambigualis (PAm)); DLM (medial part of the dorsolateral thalamus), LMAN (lateral magnocellular nucleus of the anterior nidopallium); MC (motor cortex). Figure 1A reproduced from [3] and Figure 1B reproduced from [2].