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Birdbrains could teach basal ganglia research a new song

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Recent advances in anatomical, physiological and histochemical characterization of avian basal ganglia neurons and circuitry have revealed remarkable similarities to mammalian basal ganglia. A modern revision of the avian anatomical nomenclature has now provided a common language for studying the function of the cortical–basal-ganglia–cortical loop, enabling neuroscientists to take advantage of the specialization of basal ganglia areas in various avian species. For instance, songbirds, which learn their vocal motor behavior using sensory feedback, have specialized a portion of their cortical–basal ganglia circuitry for song learning and production. This discrete circuit dedicated to a specific sensorimotor task could be especially tractable for elucidating the interwoven sensory, motor and reward signals carried by basal ganglia, and the function of these signals in task learning and execution.

Introduction

The cortical–basal ganglia circuit has been implicated in the learning and execution of sequences of movements [1–5]. Advancing this concept in mammals has been hindered by the complexity of the connections within the basal ganglia. Despite the general structure of functional loops connecting the cortex and basal ganglia [6,7], the complex pattern of convergent and divergent projections, and the sparse connectivity within these structures [8,9], has not enabled specific behavioral repertoires to be linked to specific circuits.

We propose that several major obstacles to understanding cortical–basal ganglia function could be reduced by using more comparative and neuroethological approaches to the problem. Birds possess virtually all mammalian basal ganglia structures, and their pallial inputs and thalamic and brainstem outputs, with some intriguing differences that could shed light on function. Moreover, a subset of birds, the songbirds, learn to produce their complex, sequenced vocal motor output using sensory feedback [10], and have specialized a portion of their forebrain–basal ganglia circuitry expressly for the purpose of song learning. Because this specialized cortical–basal ganglia circuit, known as the anterior forebrain pathway (AFP), is discrete and devoted to a specific well-defined behavior, rather than a broad range of motor behaviors, it should be particularly tractable for investigating how basal ganglia structures contribute to the learning and performance of motor skills.

Here, we review the anatomical and electrophysiological studies that support the strong parallels between avian and mammalian basal ganglia circuitry, and the functional investigations of the songbird AFP that are beginning to suggest the behavior-related signals it carries.

Avian basal ganglia and the new avian nomenclature

Modern views of the avian telencephalon

A glance at a traditional avian atlas would suggest that almost the entire avian telencephalon is basal ganglia, because most of the structures of the lateral telencephalic wall have names with the word 'striatum' as a root. However, modern neuroanatomical, molecular biological and neurochemical studies have shown that the avian basal ganglia have much the same telencephalic extent as in mammals (Figure 1). The voluminous territory above the basal ganglia in birds is now recognized as functionally and developmentally akin to the neocortex of mammals, deriving in the same way as cortex from the pallial sector of embryonic telencephalon. At an open meeting in July 2002 known as the Avian Brain Nomenclature Forum, avian brain nomenclature was revised to reflect this modern knowledge [11] (Figure 1).

The new terminology for the avian basal ganglia and its major brainstem afferent and efferent cell groups is very similar to that in mammals. For example, the basal telencephalic territory that is rich in dopaminergic fibers and cholinesterase, which in mammals is known as the striatum (i.e. caudate–putamen), is now also called the striatum in birds [12,13]. Similarly, the basal telencephalic structure that resembles mammalian globus pallidus in its neurochemistry, cytology and connections is now called the globus pallidus in birds too. Recent studies of forebrain patterning reinforce these homologies, showing that birds and mammals use the same genes during the development of the striatal, pallidal and pallial sectors of the telencephalon [14].

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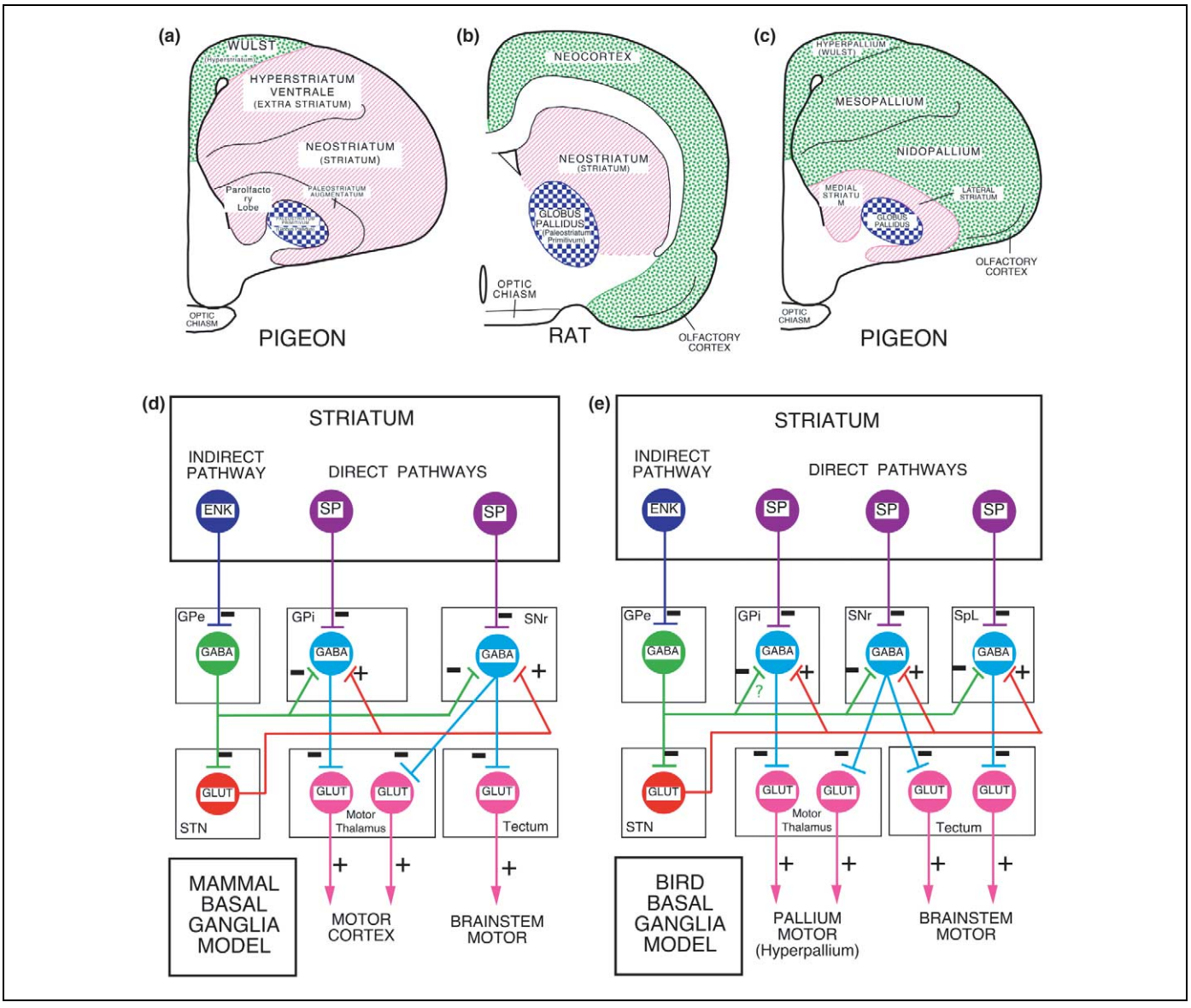

Figure 1. Schematic drawings showing the traditional and revised avian telencephalic nomenclature, a mammalian basal ganglia circuit model, and an avian basal ganglia circuit model. (a–c) Avian basal ganglia nomenclature. In traditional avian atlases, most of the structures of the lateral wall of the telencephalon have names with the word 'striatum' as a root **(a)**, stemming from terminology developed in the early 20th century, when most of the avian telencephalon was thought to consist of a hypertrophied basal ganglia. This view was part of a theory that the major subdivisions of the telencephalon had evolved in serial order: a globus pallidus (also called, because of its presumed antiquity, the paleostriatum) in jawed fish, a neostriatum in amphibians, and a primitive cerebral cortex in reptiles. Mammals were thought to have elaborated cerebral cortex into neocortex **(b)**, and birds were thought to have elaborated the basal ganglia by addition of a new territory known as the hyperstriatum (a). This view of telencephalic evolution has been refuted by modern neuroanatomical, molecular biological and neurochemical studies. It is now clear that the basal ganglia are not hypertrophied in birds but, rather, occupy much the same telencephalic extent as in mammals **(c)**. The large territory above the basal ganglia in birds is now realized to be functionally and developmentally akin to the neocortex of mammals. To reflect such current understanding better, avian telencephalic terminology was recently revised [11]. **(d,e)** Circuit diagrams comparing the functional organization of the basal ganglia in mammals and birds. The pluses and minuses indicate whether specific projections use an excitatory (+) or inhibitory (−) neurotransmitter. The characteristic transmitter used by each major type of projection neuron, which might not be the primary neurotransmitter (e.g. in the case of striatal projection neurons), is also shown. The terminology used for basal ganglia subdivisions in birds is now similar to that in mammals, as per the recent revision in avian brain nomenclature. As in mammals, the striatal and pallidal output circuitry of birds is organized into direct substance P (SP)-positive striatal outputs to pallidal neurons promoting movement and enkephalin (ENK)-positive striatal outputs to pallidal neurons inhibiting unwanted movement. The pallidal neurons of the indirect pathway have direct outputs to the targets of the SP-expressing striatal neurons [i.e. internal segment of globus pallidus (GPi), substantia nigra pars reticulata (SNr) and nucleus spiriformis lateralis (SpL)] and indirect outputs to the same targets via the subthalamic nucleus (STN). In mammals, SP-expressing neurons target two populations of pallidal-type neurons (GPi and SNr), whereas in birds three populations are targeted (GPi, SNr and SpL). However, it is not yet certain whether neurons resembling those of the globus pallidus external segment (GPe) in the avian globus pallidus (where they are intermingled with GPi-type neurons) have a projection to GPi-type neurons of the avian globus pallidus. Such a projection has been demonstrated in mammals [93]. The striatum in mammals receives extensive dopaminergic input from the midbrain, and excitatory glutamatergic (GLUT) input from the thalamus and cerebral cortex. Striatal inputs are similar in birds, with a massive dopaminergic input from the midbrain, an excitatory glutamatergic input from the thalamus, and an excitatory glutamatergic input from most of the pallium overlying the striatum, corresponding to the corticostriatal circuit of mammals. Panels (a–c) reproduced, with permission, from [11]; (e) reproduced, with permission, from [18].

Circuitry of avian basal ganglia

In both birds and mammals, the basal ganglia consist of the same set of interneuron and projection-neuron types [15]. Striatal projection neurons include two main intermingled types in both birds and mammals: those containing substance P, dynorphin and GABA, and those containing enkephalin, neurotensin and GABA [15–17]. These neuron types give rise to projections to the midbrain substantia nigra and globus pallidus, and they receive a major glutamatergic input from the overlying pallium, a

Table 1. Cell types and connectivity of avian cortical–basal ganglia projection neurons[a]

BG-related cell type in birds	Location in birds	Transmitter used	Source of input	Projection target	Location of comparable cell type in mammals	Refs
IT-type corticostriatal neuron	External pallium and nidopallium	Glutamate	Pallium	Striatum	Layers 3 and upper 5 of neocortex	[23]
PT-type corticostriatal neuron	Hyperpallium and arcopallium	Glutamate	Pallium	Striatum	Lower layer 5 of neocortex	[23]
SP+ striatal projection neuron	Striatum	GABA	Pallium	GPi neurons of globus pallidus, SNc and SNr	Striatum	[15]
ENK+ striatal projection neuron	Striatum	GABA	Pallium	GPe neurons of globus pallidus	Striatum	[15]
GPi-type pallidal neuron	Globus pallidus	GABA	SP+ striatal neurons	Ventrointermediate anterior thalamus	GPi	[15]
GPe-type pallidal neuron	Globus pallidus	GABA	ENK+ striatal neurons	Subthalamic nucleus	GPe	[15]
Thalamic–M1 projection neuron	Ventrointermediate anterior thalamus	Glutamate	GPi-type neurons of globus pallidus	M1 of the hyperpallium	Ventral anterior and lateral thalamus	[15]
Subthalamic–pallidal neuron	Subthalamic nucleus	Glutamate	GPe-type neurons of globus pallidus	GPi-type pallidal neurons	Subthalamic nucleus	[18]
'Cortical' pyramidal tract neuron	M1 of hyperpallium	Glutamate	Ventrointermediate anterior thalamus	Brainstem premotor and cord motor neurons	Motor cortices	[15]
A9 dopaminergic neuron	SNc	Dopamine	SP+ striatal neuron	Striatum	SNc	[15]
Nigrothalamic and nigrotectal neurons	SNr	GABA	SP+ striatal neuron	Ventrointermediate anterior thalamus and tectum	SNr	[15]

[a]Abbreviations: BG, basal ganglia; ENK+, enkephalin-containing; GPe, external segment of globus pallidus; GPi, internal segment of globus pallidus; IT-type, intratelencephalically-projecting type; PT-type, pyramidal tract-type; SNc, substantia nigra pars compacta; SNr, substantia nigra pars reticulata; SP+, substance P-containing.

major dopaminergic input from midbrain, and a lesser glutamatergic input from thalamus (Table 1). These two types of striatal projection neuron, a substantia nigra and a globus pallidus are present in all jawed vertebrates, supporting the idea that the basal ganglia performs a fundamental role in telencephalic function. Striatal interneuron types are also common to birds and mammals (Table 2). Moreover, avian basal ganglia circuitry is organized in the same direct–indirect pathway plan as in mammals (Figure 1), with the subthalamic nucleus probably being crucial to the interactions of these two basal ganglia circuits [18].

These similarities suggest that study of the basal ganglia of birds can aid in understanding the mammalian basal ganglia. Moreover, organizational differences between birds and mammals could be exploited. For example, in mammals, striatonigral neurons and striatopallidal neurons are intermingled, making it difficult to study them separately. In birds, however, striatonigral neurons occupy the medial striatum whereas striatopallidal neurons occupy lateral striatum, which simplifies distinguishing them [19,20]. Similarly, in mammals two types of corticostriatal neuron are found in all cortical areas – a type in upper layer 5 and layer 3 that projects only intratelencephalically (IT-type) and a type in deep layer 5 that projects to the pyramidal tract (PT-type) [21,22]. Because of their close proximity, these two cell types are difficult to study separately in mammals; in birds, these cell types are found in separate parts of the pallium [23,24]. Finally, songbirds possess a specialized cortical–basal ganglia circuit involved in song learning. The specialization of this circuit could help link basal ganglia function to behavior. The anatomy and physiology of this circuit will now be detailed.

Table 2. Cell types and connectivity of songbird Area X[a]

Cell type [26]	Morphology [26]	Neurochemical	Connections	Physiology [26]	Mammalian homolog
Spiny	Small soma, spiny	GAD [40]	Inputs from pallial afferents, contact pallidal cells [30]	Hyperpolarized resting potential, fast inward rectification, delayed spiking	Medium spiny neuron
Fast-spiking	Aspiny	NR	NR	Very fast firing rates	Parvalbumin fast-spiking interneuron
Cholinergic	Large, aspiny	ChAT [26]	NR	Long-lasting afterhyperpolarization, slow spontaneous firing	Cholinergic interneuron
Low-threshold spike	Aspiny	NR	NR	Broad, low-threshold spike	SST+, NOS+ interneuron
Aspiny fast-firing (pallidal)	Large, sparsely spaced	Express GAD [40] and LANT-6 [28] (but not Nkx2.1) [25]	Receive contacts from spiny neurons, project to thalamus, can also receive pallial inputs [30]	Intrinsically spontaneously active ~20 Hz	Globus pallidus projection neuron

[a]Abbreviations: ChAT, choline acetyl transferase; GAD, glutamic acid decarboxylase; NOS, nitric oxide synthase; NR, not reported; SST, somatostatin.

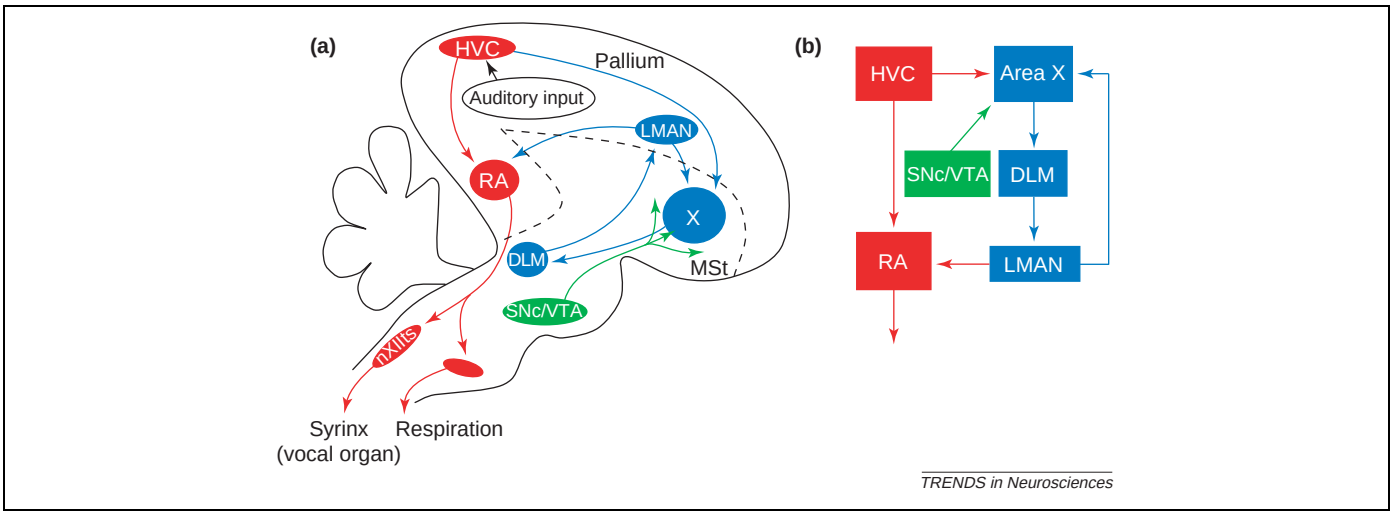

Figure 2. Simplified illustrations of song-related nuclei in oscine songbirds. **(a)** Vocal control nuclei are organized in two major pathways. Auditory inputs (largely from the song system nucleus NIf) project to the nucleus HVC. A motor pathway (red) descends from nucleus HVC to the robust nucleus of the arcopallium (RA). RA projects both to the hypoglossal nucleus (nXIIts), which innervates the syrinx (the vocal organ of birds), and to several brainstem respiratory centers. This pathway is essential for song production. A second circuit (blue), known as the anterior forebrain pathway (AFP), arises from a separate set of projection neurons in the pallial nucleus HVC. These neurons project to Area X of the medial striatum (MSt). Area X projects to the dorsolateral thalamic nucleus (DLM), which projects to the lateral magnocellular nucleus of the nidopallium (LMAN). LMAN projects back to motor circuitry at the RA, with collateral axons projecting to Area X. Dopaminergic neurons (green) from the ventral tegmental area (VTA) and the substantia nigra pars compacta (SNc) project strongly to Area X, and more weakly to LMAN (not shown). **(b)** The major pallial inputs and outputs of the AFP, and its internal connectivity. The AFP is not essential for production of songs, but is required for learning and adult song plasticity [47,49].

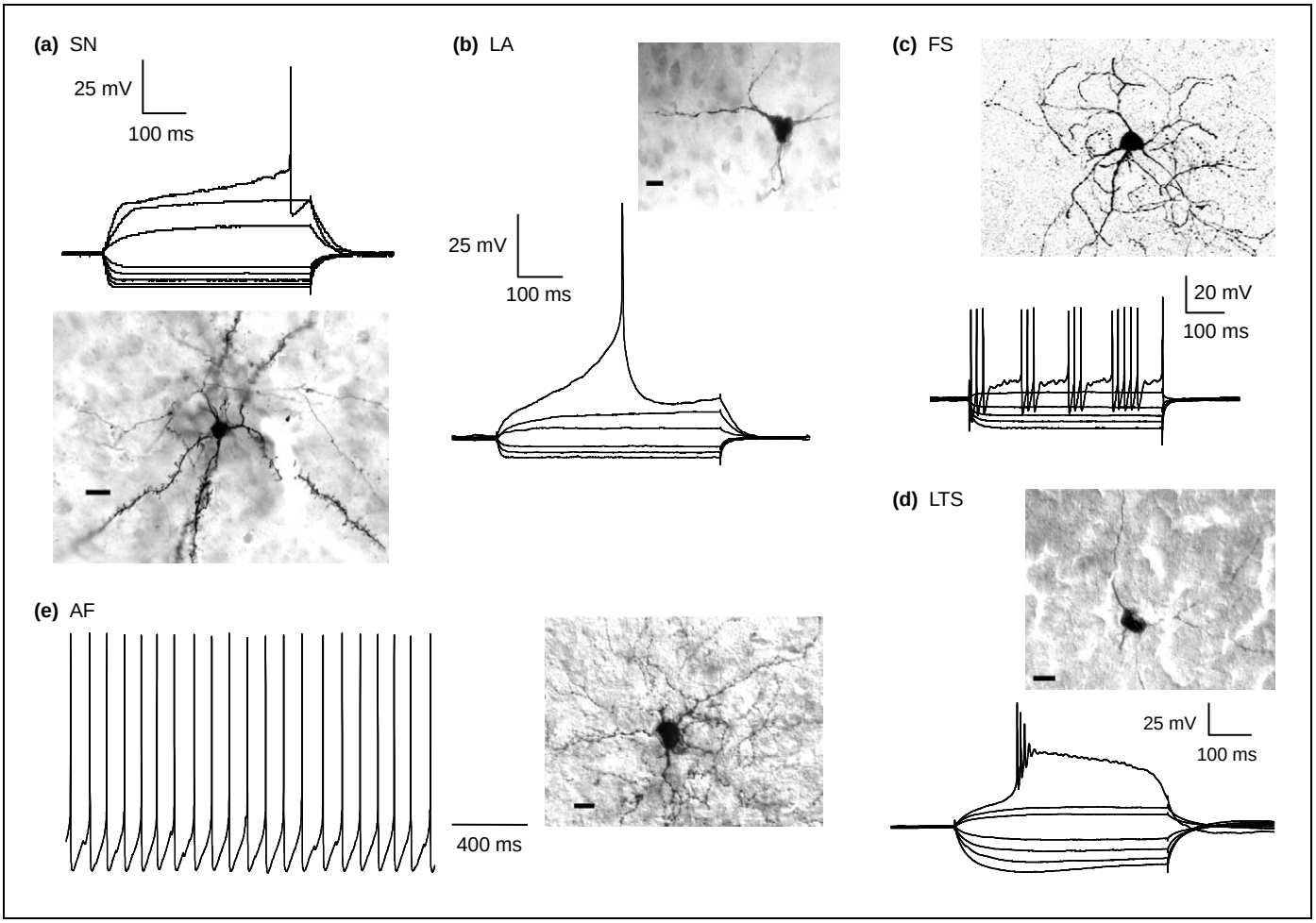

Figure 3. Cell types of Area X: electrophysiological and morphological identification. The large majority of Area X neurons resemble mammalian striatal medium spiny neurons (SN) **(a)**. Three neuron classes correspond to striatal interneurons: long-lasting afterhyperpolarization (LA) neurons, which are cholinergic **(b)**; fast spiking (FS) neurons **(c)**; and low-threshold spike (LTS) neurons **(d)**. In addition, Area X contains a cell type resembling mammalian pallidal cells and named aspiny fast-firing (AF) neurons **(e)**. Data reproduced, with permission, from [26] © (2002) Society for Neuroscience.

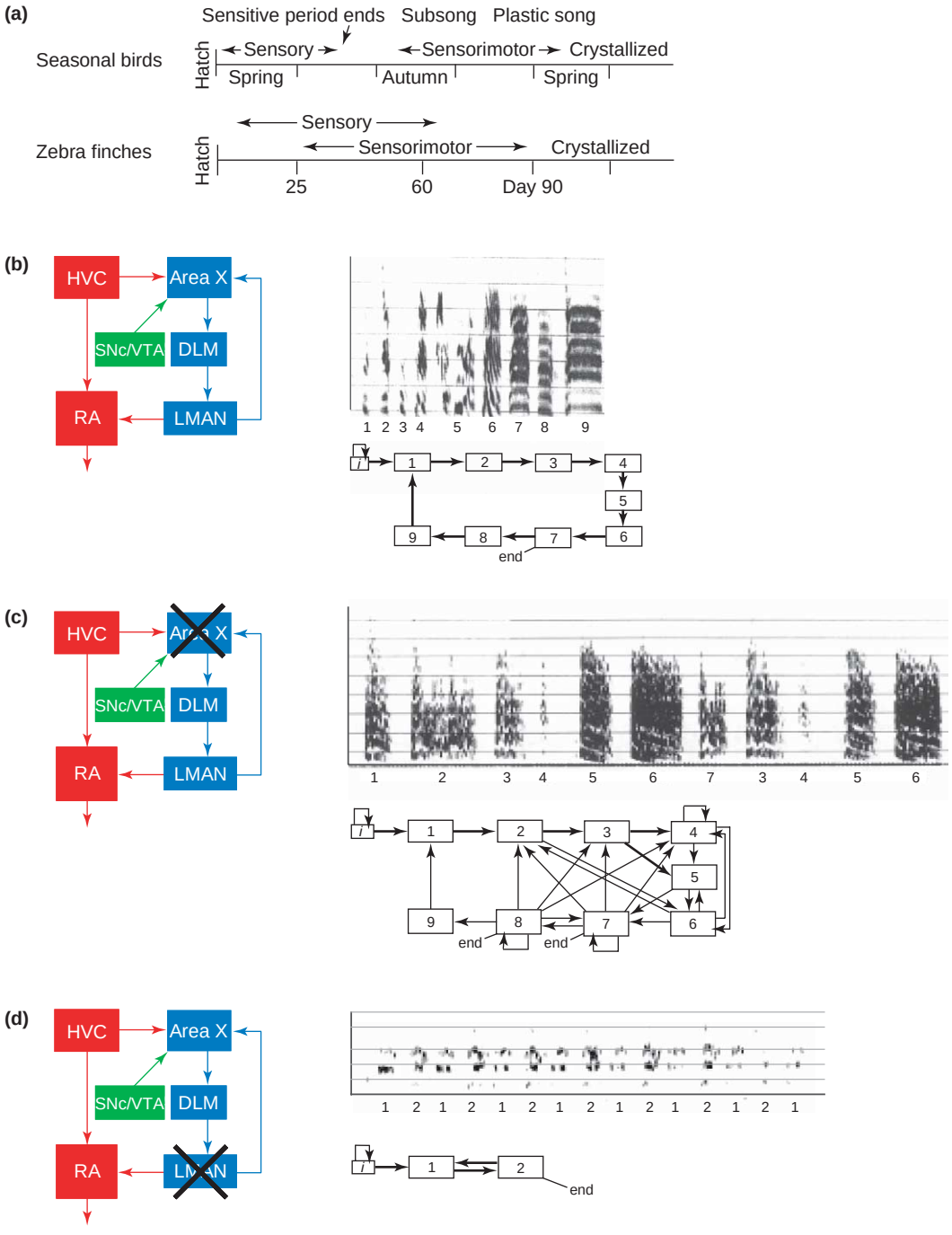

Figure 4. Song learning and behavioral effects of songbird cortical–basal ganglia lesions. **(a)** Songbirds learn their song in two phases, as shown by the timelines [10]. During an initial sensitive period for 'sensory' learning, in the first few months of life, seasonal birds memorize the adult 'tutor' song. Later, during 'sensorimotor' learning, they begin to sing immature 'subsong' and gradually match it to the stored memory of the tutor song using auditory feedback. The developing, so-called 'plastic' song eventually becomes stable or 'crystallized', and shows evidence of tutor copying, although birds also insert improvisations of their own. In zebra finches, the basic elements of song learning are the same as in other songbirds but, because these birds develop and learn very rapidly, there is overlap between the two phases of song learning. **(b)** To the right of the song-system schematic, the song of a zebra finch is shown as a spectrogram, reprinted with permission from [94], which plots frequency versus time, and indicates sound intensity by the darkness of the trace. Adult zebra finch song consists of a stereotyped sequence of syllables (indicated by the numbers) separated by short silent intervals. The stereotypy of the adult sequence is illustrated below the spectrogram by the transition diagram, which shows the typical transitions between syllables and indicates their relative frequency by the thickness of the arrows. Songs of normal zebra finches after LMAN lesions in adulthood show virtually no change in their spectrograms or sequence. **(c)** Lesions of Area X in juveniles, shown schematically on a circuit diagram at left, cause the song to stay immature and highly variable in sequence even in adulthood. The right panel shows an adult song from an Area-X-lesioned bird, with abnormally long and wavering syllables and a highly variable transition diagram. Reproduced, with permission, from [46] © (1991) Society for Neuroscience. **(d)** By contrast, LMAN lesions in juveniles cause the song to stabilize prematurely on a restricted number of abnormal syllables, shown by a spectrogram of an LMAN-lesioned bird [reproduced, with permission, from [44] © (1984) AAAS] and a simple, stable transition diagram.

Area X and the AFP for song

The AFP (Figure 2) of oscine songbirds is essential for vocal learning and plasticity. Area X, a key nucleus of the AFP, lies within the medial striatum, suggesting that the AFP is a cortical–basal ganglia circuit devoted to song-related functions. Area X receives afferents from two pallial nuclei, HVC (used as the proper name) and the lateral magnocellular nucleus of the anterior nidopallium (LMAN), and it projects to the medial portion of the dorsolateral thalamic nucleus (DLM). The AFP thus appears to form a three-station (pallium–basal ganglia–thalamus) loop, in contrast to more typical four-station (cortex–striatum–pallidum–thalamus) cortical–basal ganglia loops in mammals and in pigeons (as already discussed). We here present evidence that Area X has both striatal and pallidal components and that, despite this intermingling of cells, the basic pattern of connectivity seen in mammals is conserved.

Area X contains various cell types (Table 2), the vast majority of which are GABAergic neurons [25]. Most of these have small somata and very spiny dendrites, and exhibit intrinsic electrophysiological features closely resembling those of mammalian striatal medium spiny neurons [26]. These features include a hyperpolarized resting potential *in vitro*, fast inward rectification, and delayed action-potential firing (Figure 3). Electrophysiological and immunocytochemical studies have also revealed three classes of Area X neuron corresponding to mammalian striatal interneurons [27,28] (Figure 4). Area X thus has a full complement of striatal cells.

A final cell type of Area X is the aspiny fast-firing (AF) neuron. Based on electrophysiological, morphological and immunocytochemical properties, AF cells do not correspond to any mammalian striatal class; rather, they correspond to a class of pallidal cell [29] (Figure 3). At least some of these neurons probably project to DLM [30]. Moreover, these projection neurons express glutamic acid decarboxylase (GAD) [31] and the neurotensin-related peptide LANT6, as do mammalian pallidal neurons [28]. They do not, however, express the mammalian pallidal marker Nkx2.1 [25].

The connectivity of Area X also exhibits both striatal and pallidal features. Afferents from the pallial areas HVC and LMAN make glutamatergic connections, mediated by AMPA and NMDA receptors, onto Area X spiny neurons [32]. Area X receives dense dopaminergic innervation from the midbrain, including the ventral tegmental area (VTA) [33,34]. The spiny neurons of Area X contact the pallidal neurons [28,30], suggesting that song-related information can be transmitted via the AFP circuit in a fashion resembling that of the mammalian direct pathway. The Area X projection to DLM ends as strongly inhibitory, calyx-like GABAergic synaptic contacts, with one such synapse per DLM neuron [31].

Dopamine affects intrinsic and synaptic properties in Area X. D_1 receptor activation enhances spiny neuron excitability and D_2 receptor activation reduces excitability [35]. Dopamine has diverse actions on different spiny neurons, suggesting that most spiny neurons express both D_1 and D_2 receptors and that, on average, D_2 receptors are more numerous or effective. D_1 receptor activation presynaptically depresses pallial synaptic inputs [32] and D_1 receptors are essential for long-term potentiation (LTP) in Area X [36].

Thus, a striking number of the cellular and physiological components of the striatum and pallidum are found in Area X, but are merged into one structure rather than being segregated, as in mammals and in the avian lateral striatum and pallidum. It is tempting to speculate that such heterogeneity of basal ganglia organization, both within and across species, is facilitated by the developmental history of the basal ganglia, which involves extensive migration and cellular intermixing [37,38].

Although recent work has focused on Area X, the AFP as a whole also resembles a cortical–basal ganglia circuit. As in mammals: there is marked topography throughout the AFP [39]; the thalamic DLM neurons show typical thalamic properties, including regular firing from rest, and burst firing from hyperpolarized potentials [40,41]; and the projection from thalamus to LMAN, corresponding to a mammalian thalamocortical projection, is glutamatergic [42]. It remains to be seen whether Area X also participates in an equivalent of the mammalian indirect pathway, via the subthalamic nucleus. More studies on mammals will also clarify whether, as in DLM, pallidal 'inhibitory' inputs to the thalamus can drive postsynaptic firing with precise timing [43].

Because the AFP is a basal ganglia circuit, but appears to mediate a discrete sensorimotor task, it could facilitate mapping of behavior onto specific neurons and their properties, and it could ultimately elucidate basic neural algorithms of basal-ganglia-dependent learning. Functional studies of the AFP in behavior are summarized in the next section.

Songbird basal ganglia in action

AFP function in learning of behavior

Songbirds learn their complex, sequenced vocal motor behavior (Figure 4b) in early life, in a process (Figure 4a) with parallels to human speech learning, especially in its marked dependence on hearing self and others. The AFP is crucial for this learning. Lesions of Area X (the striatal–pallidal portion of the AFP) or of LMAN [the AFP outflow nucleus, equivalent to cortical targets of the mammalian basal ganglia (Figure 2)] both result in dramatic disruption of song when the lesions are made early in sensorimotor learning [44–46]: Area X lesions lead to failure of song stabilization and production of a continually varying sequence of syllables [45,46] (Figure 4c), whereas LMAN lesions cause the song to stabilize prematurely into a simplified sequence of abnormal syllables [44,46] (Figure 4d). These differences are likely to reflect the structure of the AFP:LMAN lesions result in complete withdrawal of AFP activity from the descending motor pathway, whereas lesions of Area X presumably retain input from LMAN to motor circuitry, but strip this area of afferent information, and perhaps increase its activity abnormally owing to removal of inhibitory outflow from Area X [31,46].

Although AFP lesions in normal adult finches have less disruptive effects on song than do juvenile lesions [44] (Figure 4b), the AFP does function in adults. For instance,

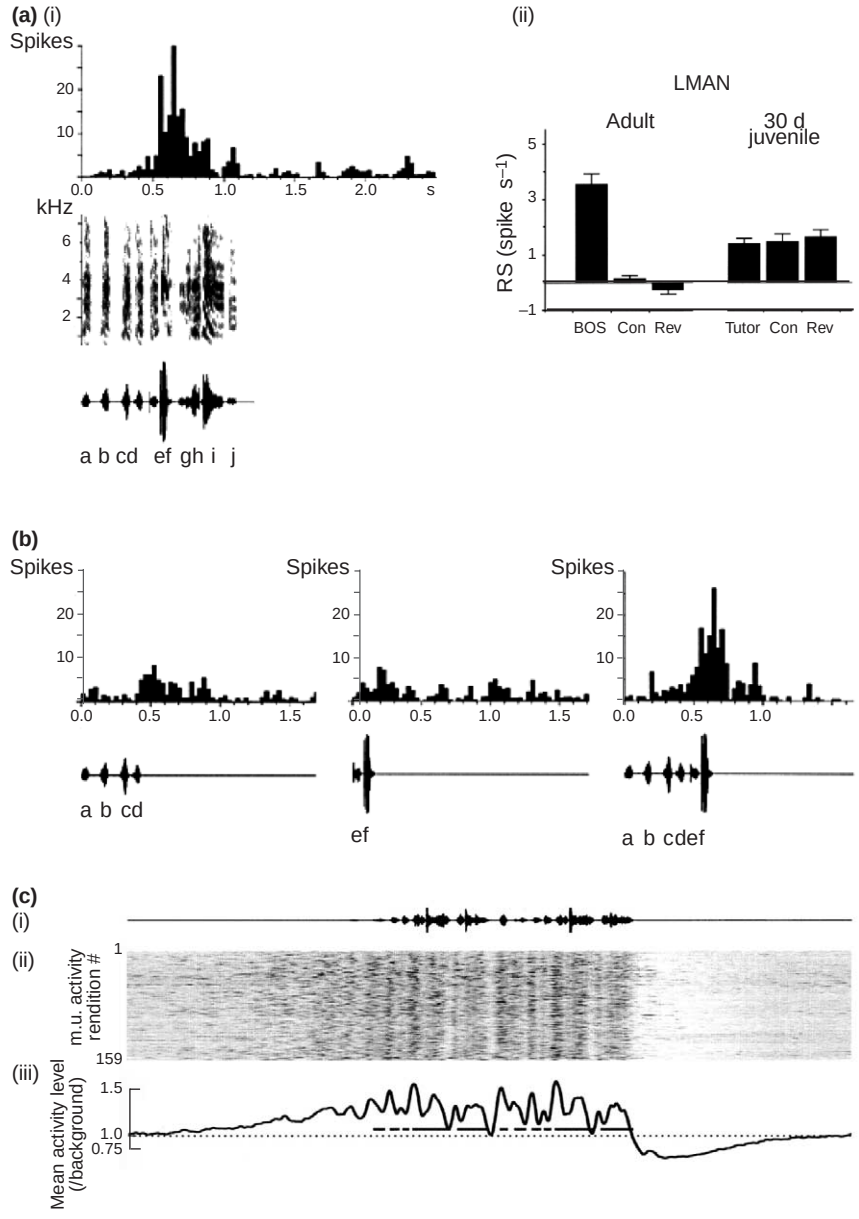

Figure 5. Sensory and motor properties of songbird cortical–basal ganglia circuits. **(a)** (i) A peristimulus time histogram (PSTH) illustrates the marked response of a typical single neuron in the lateral magnocellular nucleus of the nidopallium (LMAN) to playback of the bird's own song (BOS); song is depicted both as a spectrogram and as an oscillogram (plot of amplitude versus time), with the song syllables indicated by lower case letters. (ii) The histograms of average LMAN responses show that in adults, LMAN auditory neurons exhibit much larger response strengths (RS; mean stimulus-evoked response minus background) to BOS than to conspecific song (Con) or reversed versions of BOS (Rev). By contrast, in young, pre-singing birds (30 days of age), these neurons respond equivalently to tutor song, unfamiliar conspecific song (Con), or reversed versions of tutor song (Rev). **(b)** The auditory neuron shown in (a) is combination-sensitive, as illustrated by PSTHs of its response to the indicated combinations of syllables. Presentation of the first four syllables alone elicits little response; the following two syllables in isolation also elicit only a weak response. In combination, however, the stimuli a–f elicit a strong response that not only exceeds the sum of responses to stimuli a–d and e–f, but is as strong as the response to the entire song. **(c)** Singing-related activity in LMAN. (i) Oscillogram of the song produced by the bird (i), and the mean multi-unit (m.u.) activity in LMAN before, during and after each of 159 renditions of the song, aligned to the song (ii). Activity level is represented by a color scale, where black indicates high neural activity, and white low activity. (iii) Mean of the activity of all the renditions above, illustrating the onset of activity before sound, and the peaks of activity relative to syllables, which are indicated by black bars. The duration of the entire panel is 4.5 s. Data in (a) and (b) reproduced, with permission, from [57]; data in (c) reproduced, with permission, from [95] © (2002) National Academy of Sciences, USA.

LMAN lesions prevent the deterioration of adult song that normally follows deafening [47] or disruption of the vocal apparatus [48]. Because adult LMAN lesions prevent changes in song triggered solely by deafening, it is possible that the AFP evaluates sensory feedback of song, and that aberrant AFP information generated in response to altered or absent feedback actively drives non-adaptive changes in song [49]. This hypothesis suggests that there are parallels between the effects of LMAN lesions in deaf adult birds and those of pallidotomy in Parkinson's disease: in both cases, when motor behaviors are already well-learned, removal of presumed abnormal cortical–basal ganglia activity enables more normal expression of these behaviors. During learning, activity in these same circuits could instruct adaptive changes in motor output. Testing this hypothesis awaits more information about the signals carried by the AFP both during learning and in abnormal conditions. Such experiments will also test ideas from studies of mammalian cortical–basal ganglia function – for instance, that basal ganglia circuits select one

motor action (e.g. a particular song syllable) while inhibiting competing motor programs [50], or that the balance between direct and indirect pathways influences movement [4,51].

Sensory and motor properties of songbird cortical–basal ganglia neurons

As in mammals [52–55], songbird basal ganglia appear to have both sensory and motor-related responses. In anesthetized adult zebra finches, neurons in the AFP, and in its pallial inputs and motor output areas, respond highly selectively to playback of the bird's own song (BOS) relative to songs of other individuals. These neurons are also often 'combination-sensitive' – that is, they respond more strongly to the correct sequence of sounds in song than to component sounds played alone or in altered order [56,57] (Figure 5a,b). This is an intriguing property for circuits crucial to sequence learning, with striking parallels to the sequence-specific neurons observed in mammalian cortical–basal ganglia circuits [58,59].

Moreover, this 'song-selectivity' emerges during, and reflects, learning of the BOS (Figure 5a) [57,60]. In some cases, neurons of the AFP also respond strongly to the tutor song copied by the bird [60]; such selectivity could be useful in the BOS–tutor song comparison that is crucial to song learning.

Both LMAN and Area X neurons, like their counterparts in mammalian cortex and basal ganglia [52,53], also carry motor-related signals. They fire vigorously throughout singing in adult zebra finches [61,62] (Figure 5c), despite the fact that they are not required for normal adult song production (Figure 4b) [44–46]. AFP activity during singing resembles multi-unit activity during singing in the song motor control nucleus HVC [63,64], and persists even in deafened birds [61]. This suggests that singing-related AFP activity represents in part an efference copy of the premotor signals also sent to the motor output pathway (Figure 2), which could be useful during learning [65]. Recent experiments in which microstimulation of LMAN resulted in acute and specific changes in learned parameters of adult song [66] demonstrate that AFP activity can direct real-time changes in song. They also support the idea that in birds learning to sing, AFP signals could bias song towards particular vocal motor targets.

Finally, similar to activity in basal ganglia neurons and their cortical inputs and outputs [55,67–69], AFP neuronal activity is strikingly modulated by context. Birds sing in two contexts, either alone ('undirected' song) or socially ('directed' song), usually to a female companion as part of courtship. Activity in the AFP is dramatically different in these two settings: during directed singing, activity in both Area X and LMAN is much lower than during undirected singing [62,70], and its variability in timing across trials and in relation to song is markedly decreased [70]. This suggests that social context triggers an increase in signal-to-noise ratio in AFP firing, decreasing the amount of activity overall but enhancing its precision. AFP variability is correlated with variability in song output, and if LMAN is lesioned, the song loses its social-context-driven variation [66]. This provides further evidence for real-time modulation of song by the AFP, and raises the possibility that cortical–basal ganglia circuits such as the AFP also contribute to motor learning by introducing variability important for reinforcement learning.

An obvious candidate for a behaviorally-sensitive modulator of AFP firing is the strong dopaminergic input from midbrain areas, especially the VTA, to Area X and LMAN [71]. Courtship is an arousing and potentially reinforcing setting, known to trigger dopamine release in other species [72,73], and the alteration in Area X and LMAN firing with social context is reminiscent of the striking changes in the signal-to-noise ratio of firing seen in slices of mammalian striatum in response to D_1 agonists [35,74].

Neuronal correlation

Mammalian basal ganglia circuits have extensive anatomical convergence and divergence of inputs from the cortex onto the striatum, and thence to the pallidum [9], in addition to mutual interconnections among neurons within several stages of the circuit. Such architecture predicts correlated firing among projection neurons within the cortex and striatum. However, only sparse evidence for such neuronal interactions has been observed, perhaps because functional correlations depend on task-related rather than topographic relationships among inputs [75–77]. Task-dependent firing relationships would not necessarily be present in neighboring or randomly sampled neurons [78]. However, in anesthetized adult zebra finches there is striking correlation of activity between many pairs of neurons across nuclei of the AFP and its inputs and outputs [79]. Anatomically, the songbird cortical–striatal circuit resembles that of mammals, with wide convergence and divergence of inputs, and recurrent interconnectivity within AFP nuclei [80–83]. In contrast to mammals, however, this architecture also apparently enables strong functional correlations. The concentration in the songbird AFP of neurons specialized for vocal motor control could facilitate selective recording from neurons that are involved in a common task, and thus are functionally interconnected.

Cellular plasticity in the song system

Cellular mechanisms that could contribute to learning occur in at least two nuclei of the songbird AFP. Collateral synapses within the pallial nucleus LMAN show activity-dependent LTP [80]. This form of plasticity depends on postsynaptic action-potential timing and on activation of NMDA receptors, which undergo striking developmental changes in this nucleus [84]. LMAN LTP occurs in 20-day-old zebra finches, at an age when birds can be memorizing the tutor song but are not yet singing. However, it is not observed in slices from 60-day-old birds, which have completed song memorization and are in the middle of the sensorimotor phase of song learning. Another form of LTP occurs at synapses made by pallial afferents to Area X spiny neurons [36]. This LTP is Hebbian and synapse-specific, requires activation of both NMDA receptors and D_1 receptors, and resembles plasticity reported in striatum [85]. This form of plasticity is not found in slices from 30-day-old finches, but occurs from at least day 47 through

Box 1. Outstanding questions

Several important questions about basal ganglia function might be more easily addressed in songbird systems. Space restrictions limit us to a few suggestions:

1. Function of different components of cortical–basal ganglia loops

Basal ganglia circuits have been hypothesized to be crucial in motor-sequence learning, in part based on their response properties [87]. However, in many cases, studies of the cortical areas that project to the striatum show strikingly similar properties [88], and inactivation of cortical areas such as the supplementary and presupplementary motor areas causes deficits in learning of motor sequences that resemble deficits resulting from inactivation of the basal ganglia [89]. Thus, the unique contribution of each part of the cortical–basal ganglia circuit to sequence learning remains unclear. Understanding this will require simultaneous recordings in functionally corresponding areas of the cortex and basal ganglia as animals learn a sequenced motor task, and recordings in one area paired with manipulations of activity in another. Such experiments should be simpler both to carry out and to interpret in the functionally specialized pallial–basal ganglia circuit devoted to song [39]. Results could provide further evidence for the idea, gradually emerging from mammalian systems, that it is most accurate to think of the function of cortical–basal ganglia loops as a whole, and that learning emerges from the mutual interaction between cortex and basal ganglia. Another important question in songbirds is whether (and if so, how) cerebellar circuits, which seem likely to be crucial to aspects of song motor learning, interact with basal ganglia pathways, as they do in mammals.

2. Sensory and motor interaction in cortical–basal ganglia circuits

Cortical–basal ganglia neurons carry both sensory and motor-related signals, but the relationship between these, which is probably crucial to circuit function, is ill-understood. In the song system, this relationship could be clearer. For instance, in the robust nucleus of the arcopallium (RA), the same neurons that exhibit song-selective responses in sleeping birds are active during singing [56]. Moreover, there is a remarkable correspondence between the auditory responses of these neurons to song and their premotor activity – playback of one set of syllables triggers an auditory response that resembles the premotor activity for the next syllable in the song. Thus, the auditory response can be considered a prediction of the motor command for the following syllable. These results raise the possibility that song-selective neurons are crucial in linking sensory and motor representations in the song system. Further investigation will need to focus on how this sensory–motor correspondence emerges, both during learning and in different parts of the circuit.

3. Dopamine in motor learning and reinforcement, and disease models

A plethora of evidence, including the effects of pathological states such as Parkinson's disease (PD), points to the importance of dopamine in motor learning, but the cellular and circuit details remain largely unclear. Experiments to examine these questions in song learning, including stimulation and lesion of dopamine inputs to the song system at crucial times during song development, if coupled with neural recordings, could be highly informative. Moreover, increasing understanding of the molecular events underlying PD [90] has enabled new models of this disease, from rodents to flies. Avian models of PD could ultimately be as useful as rodent models.

4. Function of correlated activity in cortical–basal ganglia circuits

The songbird cortical–basal ganglia loop could be ideal for studying the role of correlated activity in information propagation, because of the relatively large (compared with mammals) proportion of neurons involved in a specific sensorimotor task. It remains to be seen whether the striking correlations in anesthetized songbirds persist in the awake, behaving state. State dependence of correlations seems generally to be important in cortical–basal ganglia circuits. In dopamine-depleted monkeys, the normally weakly interconnected globus pallidus neurons become strongly synchronized [91], as do motor cortex neurons [92]. This suggests that connectivity that is normally physiologically downregulated is enhanced in this pathological state. In songbirds too, the degree of correlation in the AFP varies in its strength [79], and correlation strength in the awake songbird AFP might depend on behavior and/or dopamine levels. For instance, the degree of correlation might vary between directed and undirected singing, or between situations where the young bird sings a well-learned version of his song versus an imperfect version. Because the link to behavior can be made so much more easily than in less specialized animals, the song system could be especially well-suited to assessing the effects of cortical–basal ganglia correlations, and of modulation of correlation strength, on function.

adulthood, roughly paralleling the arrival of dopamine inputs from the midbrain [86]. These phenomena provide further evidence for similarities in cellular mechanisms between avian and mammalian basal ganglia circuits. Moreover, the well-studied learning process for songbird vocalizations, and the ability to alter learning with behavioral and circuit manipulations, offer advantages for studying how synaptic changes contribute to learning in this system.

Concluding remarks

In conclusion, the recent advances in avian basal ganglia research, together with the revolution in avian neuroanatomical nomenclature, illustrate the usefulness of avian models for the study of cortical–basal ganglia function. Whereas the complexity of mammalian basal ganglia circuitry makes several experiments technically infeasible, the specialization of nuclei for specific behaviors in songbirds should facilitate investigation of the neuronal computations underlying sensorimotor tasks, including the interrelationship of sensory and motor components and the role of dopamine in reinforcement (Box 1).

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