

- 29 Olzak, L. and Thomas, J.P. (1999) Neural recoding in human pattern vision: model and mechanisms. *Vis. Res.* 39, 231–256
- 30 Deutch, D. and Feroe, J. (1975) Disinhibition in pitch memory. *Percept. Psychophys.* 17, 320–324
- 31 Magnussen, S. *et al.* (1991) Stimulus-specific mechanisms of visual short-term memory. *Vis. Res.* 31, 1213–1219
- 32 DeValois, R.L. (1991) Orientation and spatial frequency selectivity: properties and modular organization. In *From Pigments to Perception. Advances in Understanding Visual Processes* (Valberg, A. and Lee, B.B., eds), pp. 239–247, Plenum Press
- 33 Schiller, P. H. (1995) Effect of lesions in visual cortical area V4 on the recognition of transformed objects. *Nature* 376, 342–344
- 34 Greenlee, M.W. and Thomas, J.P. (1993) Simultaneous discrimination of the spatial frequency and contrast of periodic stimuli. *J. Opt. Soc. Am. A* 10, 395–404
- 35 Chua, F.K. (1990) The processing of spatial frequency and orientation information. *Percept. Psychophys.* 47, 79–86
- 36 Vincent, A. and Regan, D. (1995) Parallel independent encoding of orientation, spatial frequency, and contrast. *Perception* 24, 491–499
- 37 Magnussen, S. and Greenlee, M.W. (1997) Competition and sharing of processing resources in visual discrimination. *J. Exp. Psychol. Hum. Percept. Perform.* 22, 1603–1616
- 38 Greenlee, M.W. and Magnussen, S. (1998) Limited capacity mechanisms of visual discrimination. *Vis. Res.* 38, 375–385
- 39 Magnussen, S. *et al.* (1996) Parallel processing in visual short-term memory. *J. Exp. Psychol. Hum. Percept. Perform.* 22, 202–212
- 40 Van Essen, D. C. and DeYoe, E.A. (1995) Concurrent processing in the primate visual cortex. In *The Cognitive Neurosciences* (Gazzaniga, M.S., ed), pp. 383–400, MIT Press
- 41 Squire, L.R. and Zola-Morgan, E.R. (1991) *Memory. From Mind to Molecules*, Freeman
- 42 Greenlee, M.W. *et al.* (1993) Delayed pattern discrimination in patients with unilateral temporal lobe damage. *J. Neurosci.* 13, 2565–2574
- 43 Greenlee, M.W. *et al.* (1995) Visual short-term memory for stimulus velocity in patients with unilateral posterior brain damage. *J. Neurosci.* 15, 2287–2300
- 44 Greenlee, M.W. *et al.* (1997) Visual discrimination and short-term memory for random patterns in patients with a focal cortical lesion. *Cereb. Cortex* 7, 253–267
- 45 Cabeza, R. and Nyberg, L. (1997) Imaging cognition: an empirical review of PET studies with normal subjects. *J. Cogn. Neurosci.* 9, 1–26
- 46 Gabrieli, J.D.E. (1998) Cognitive neuroscience of human memory. *Annu. Rev. Psychol.* 49, 87–115
- 47 Fuster, J.M. (1997) Network memory. *Trends Neurosci.* 20, 451–459
- 48 Bruckner, R.L. *et al.* (1998) Functional-anatomic correlates of object priming in humans revealed by rapid presentation event-related fMRI. *Neuron* 20, 285–296
- 49 Orban, G.A. *et al.* (1997) Human brain activity related to orientation discrimination. *Eur. J. Neurosci.* 9, 246–259
- 50 Dupont, P. *et al.* (1998) Regions in the human brain activated by simultaneous orientation discrimination: a study with positron emission tomography. *Eur. J. Neurosci.* 10, 3689–3699
- 51 Orban, G.A. *et al.* (1998) Human brain activity related to speed discrimination tasks. *Exp. Brain Res.* 122, 9–22
- 52 Cornette, L. *et al.* (1998) Human brain regions involved in direction discrimination. *J. Neurophysiol.* 79, 2749–2765
- 53 Reinvang, I. *et al.* (1998) Neocortical areas underlying visual short-term memory: evidence from fMRI. *NeuroImage* 7, S846
- 54 Sherg, M. and Berg, P. (1996) New concepts of brain source imaging and localization. *Electroencephal. Clin. Neurophysiol.* 4, 127–137
- 55 Semal, C. and Demany, L. (1991) Dissociation of pitch from timbre in auditory short-term memory. *J. Acoust. Soc. Am.* 89, 2404–2410
- 56 Walk, H.A. and Johns, E.E. (1984) Interference and facilitation in short-term memory for odors. *Percept. Psychophys.* 36, 508–514
- 57 Damasio, A.R. (1989) Time-locked multiregional retroactivation: a systems-level proposal for the neural substrates for recall and recognition. *Cognition* 33, 25–62
- 58 Magnussen, S. and Dyrnes, S. (1994) High-fidelity perceptual long-term memory. *Psychol. Sci.* 5, 99–102
- 59 Stromeyer, C.F. and Pstotka, J. (1970) The detailed texture of eidetic images. *Nature* 225, 346–349
- 60 Lages, M. and Treisman, M. (1998) Spatial frequency discrimination: visual long-term memory or criterion setting? *Vis. Res.* 38, 557–572
- 61 Kosslyn, S.M. *et al.* (1999) The role of area 17 in visual imagery: convergent evidence from PET and rTMS. *Science* 284, 167–170

Acknowledgements
The author's research is supported by the Norwegian Research Council (MH) and the Alexander von Humboldt-Stiftung (Bonn, Germany). The author thanks L. Spillmann for his comments and T. Edesstad for assistance with graphics.

Seasonal plasticity in the adult brain

Anthony D. Tramontin and Eliot A. Brenowitz

Seasonal plasticity of structure and function is a fundamental feature of nervous systems in a wide variety of animals that occupy seasonal environments. Excellent examples of seasonal brain changes are found in the avian song control system, which has become a leading model of morphological and functional plasticity in the adult CNS. The volumes of entire brain regions that control song increase dramatically in anticipation of the breeding season. These volumetric changes are induced primarily by vernal increases in circulating sex steroids and are accompanied by increases in neuronal size, number and spacing. In several species, these structural changes in the song control circuitry are associated with seasonal changes in song production and learning. Songbirds provide important insights into the mechanisms and behavioral consequences of plasticity in the adult brain.

Trends Neurosci. (2000) 23, 251–258

THE ANATOMY of the adult vertebrate brain was once believed to remain relatively static throughout an individual's lifespan (age-related neuron loss notwithstanding). In the early 1960s, however, two reports suggested the need to revise this widely held view. In 1962, Joseph Altman observed neuron proliferation in the adult rodent brain¹ and in 1964, Edward Bennett and his colleagues reported that environmental enrichment produced a subtle but significant increase in cortical mass in adult rodents². These studies suggested that anatomical plasticity persists in the brain long after

early ontogeny. Almost two decades later, Fernando Nottebohm confirmed this hypothesis by demonstrating dramatic seasonal morphological changes of entire brain regions that control song behavior in canaries (*Serinus canarius*)³.

Nottebohm's discovery stimulated much research describing seasonal changes in the nervous systems of a wide variety of adult animals. Seasonal plasticity of structure and function is now known to be a common feature of the brains of many species, particularly seasonal breeders (Table 1). These animals provide

Anthony D. Tramontin is at the Dept of Zoology, The Rockefeller University, New York, NY 10021, USA, and Eliot A. Brenowitz is at the Depts of Zoology and Psychology, and The Virginia Merrill Bloedel Hearing Research Center, University of Washington, Seattle, WA 98195, USA

TABLE 1. Comparative survey of seasonal plasticity in the adult central nervous system^a

Class	Examples	Refs
Gastropoda	Inhibitors of protein kinases A and C are most effective during the non-breeding season at suppressing egg-laying hormone secretion from the neuroendocrine bag cells of <i>Aplysia californica</i> .	4
	A greater percentage of <i>Aplysia californica</i> siphon motoneurons exhibit an excitatory response to FMRFamide treatment during the summer months.	5
Crustacea	Motor terminals that innervate the crayfish (<i>Procambarus clarkii</i>) claw-closer muscle produce smaller EPSPs, are more resistant to fatigue and have more synaptic varicosities during the summer than during the winter.	6
Osteichthyes	Androgen-receptor levels peak during spawning in the goldfish (<i>Carassius auratus</i>) brain.	7
	The size of pineal organ cell bodies increases during the fall and winter in goldfish (<i>Carassius auratus</i>).	8
Amphibia	The volume of the medial-amygdala–anterior-preoptic-complex is larger in hibernating (pre-breeding) than in post-breeding male toads (<i>Bufo japonicus</i>).	9
Reptilia	The size of the anterior-hypothalamus–preoptic area increases while the size of the ventromedial hypothalamus decreases during the breeding season in male whiptail lizards (<i>Cnemidophorus inornatus</i>).	10
Aves	The volume of the hippocampal formation and neuronal incorporation into this brain region increase during the fall in black-capped chickadees (<i>Parus atricapillus</i>).	11,12
	The volume of several song control nuclei increases during the breeding season in songbirds.	3
	GnRH immunoreactivity is decreased, and the number of axo-somatic synaptic terminals contacting GnRH neurons is greatest in photorefractory European starlings (<i>Sturnus vulgaris</i>).	13,14
Mammalia	Motoneurons in the spinal nucleus of the bulbocavernosus are larger in breeding than in non-breeding white-footed mice (<i>Peromyscus leucopus</i>).	15
	Vasopressin innervation is enhanced in various regions of the European hamster (<i>Cricetus cricetus</i>) brain during the breeding season.	16
	Preoptic GnRH neurons in the ewe receive more synaptic inputs during the breeding season.	17
	In male Siberian hamsters (<i>Phodopus sungorus</i>) that are shifted from long days to short days, the levels of neural cell adhesion molecule increase in the AH and POA, but decreases in the MBH. Polysialic acid levels are reduced in the AH and MBH of these animals.	18
	Hippocampal neuronal incorporation is greatest during the fall in Syrian hamsters (<i>Mesocricetus aruatus</i>).	19
	The volume of the hypothalamic suprachiasmatic nucleus and the number of vasopressin-immunoreactive neurons contained within it are greater during the autumn than during the summer in humans.	20

^aNote that this list is not exhaustive, but is intended to provide examples from a wide variety of taxa.

Abbreviations: AH, anterior hypothalamus; GnRH, gonadotropin-releasing hormone; MBH, mediobasal hypothalamus; POA, pre-optic area.

powerful models within which to study naturally occurring plasticity in the adult brain. No animal, however, has provided as much insight on this topic as songbirds.

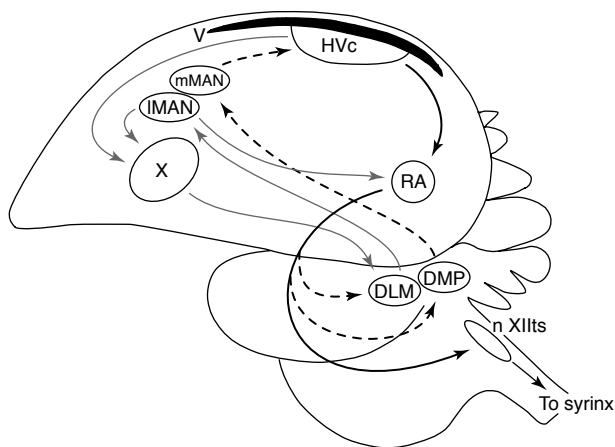
The volumes of song control nuclei change seasonally

Song is a learned behavior used by birds to attract mates and to defend breeding territories²¹. In oscine passerines (songbirds), song behavior is controlled by a network of discrete interconnected brain regions or nuclei (Fig. 1). Song behavior and the brain regions that control it are seasonally plastic in every species of seasonally breeding adult songbird that has been systematically studied^{36–39}. The entire volumes of several song nuclei, including the neostriatal region HVC (sometimes referred to as the 'high vocal center'), the robust nucleus of the archistriatum (RA) and area X of the parolfactory lobe, are considerably larger during the spring breeding season than during autumn and winter in wild birds (Fig. 1; Table 2). In the most extreme example, the volume of HVC in spotted towhees (*Pipilo maculatus*) nearly triples between the non-breeding and breeding seasons (Fig. 2). This naturally occurring plasticity in the songbird brain is perhaps the most pronounced observed in any adult vertebrate. One should note, however, that not all of the song nuclei exhibit seasonal volumetric changes. For example, these changes have not been observed in the lateral portion of the magnocellular nucleus of the anterior neostriatum (IMAN)^{37,38,40,44,45}.

Day length is the primary environmental cue that stimulates seasonal reproductive development and song

system growth^{3,38,40,44,46}. Each year prior to the breeding effort, the lengthening days of late winter and early spring stimulate gonadal recrudescence, development of secondary sexual characteristics and increases in circulating blood levels of gonadal sex steroids⁴⁷. The seasonal growth of the song control system occurs during this early stage of seasonal reproductive development, several weeks before the actual onset of breeding³⁷. Recent data suggest that the seasonal growth of the song nuclei can also be influenced by seasonal cues other than day length. In the laboratory, social cues from sexually receptive female white-crowned sparrows (*Zonotrichia leucophrys gambelii*) enhanced the photo-induced growth of two song nuclei in their male cagemates⁴⁵. HVC and RA were 20% and 15% larger, respectively, in males housed with females on long spring-like days than in males housed similarly without females. Future studies should determine whether other seasonal cues such as food availability, temperature or precipitation also influence the vernal growth of the song system.

In the laboratory, long spring-like days (LD) and elevated circulating testosterone (see below) stimulate structural changes in the song circuitry that closely resemble those observed in wild animals (Table 3). These changes occur rapidly and sequentially^{37,39,51}. In captive white-crowned sparrows, HVC volume increased by 69% within seven days of exposure to LD and testosterone. The primary efferent targets of the HVC, RA and area X, appeared to grow more slowly, only achieving full breeding volumes after 7 to 20 days of exposure to LD and testosterone. This sequential growth of the song



trends in Neurosciences

Fig. 1. The song control system is organized into two principal circuits. The main descending motor pathway (black arrows) begins in HVC (sometimes called the 'high vocal center') and terminates at the syrinx (the vocal production organ). Neuronal activity in HVC and in the robust nucleus of the archistriatum (RA) is synchronized with sound production from the syrinx^{22,23}, and inactivation of either of these nuclei abolishes song production²⁴. HVC lesions can also impair song discrimination^{25,26}. The anterior forebrain circuit (gray arrows) indirectly connects HVC to RA and is essential for song learning and perception^{23,27}. Lesions of anterior forebrain nuclei prevent normal song learning in juvenile birds^{28–30} and song perception in adult birds^{31,32}. Feedback circuits also exist within the song control system. Neurons in the lateral portion of the magnocellular nucleus of the anterior neostriatum (IMAN) that project to RA send collaterals to area X in the parolfactory lobe closing one loop. Projections from RA also initiate refferent thalamo-telencephalic loops (broken arrows) that might provide indirect feedback to HVC (Refs 33,34). The HVC receives afferent input from two song nuclei that are not shown: nucleus interfacialis of the caudal neostriatum and nucleus uvaeformis of the thalamus. HVC and RA also receive input from several auditory forebrain regions that are not shown³⁵. Finally, neurons in the lateral hypothalamus project to the dorsomedial nucleus of the posterior thalamus (DMP), which in turn projects to the medial portion of the magnocellular nucleus of the anterior neostriatum (mMAN), suggesting integration of information between the hypothalamus and the song system³³. Abbreviations: DLM, dorsolateral nucleus of the medial thalamus; nXIIIts, the tracheosyringeal portion of the hypoglossal nucleus; V, lateral ventricle.

control nuclei in adults is similar to the sequential ontogeny of these structures in juvenile birds. In young male zebra finches (*Poephila guttata*; between 12 and 53 days post-hatch), Bottjer *et al.* reported that the developmental growth of HVC preceded that of RA and area X (Ref. 52). These observations might suggest that early ontogeny and adult plasticity in the brain exploit similar mechanisms, an idea that dates back to Ramon y Cajal⁵³. Rigorous tests of this hypothesis should be carried out in a species other than the zebra finch because these birds are not typical photoperiodic seasonal breeders⁵⁴.

The sequential seasonal growth of the song control nuclei is consistent with the hypothesis that the seasonal growth of RA and area X requires trans-synaptic support from HVC. In support of this hypothesis, Brenowitz and Lent reported preliminary data that lesions of HVC blocked the seasonal growth of RA and area X in captive white-crowned sparrows⁵⁵. This result is also reminiscent of developmental studies where HVC lesions in juvenile male zebra finches blocked the full development of RA and area X (Refs 56,57). In young male zebra finches, HVC neurons produce brain-derived neurotrophic factor (BDNF), which appears to be trans-

TABLE 2. Seasonal plasticity of song control nuclei in male songbirds captured in the wild

Species ^a	HVC ^b	RA ^b	Area X ^b	Ref.
Spotted towhee (<i>Pipilo maculatus</i>)	2.88	2.35	1.60	40
Western song sparrow (<i>Melospiza melodia morphna</i>)	1.54	1.46	1.31	37
Nuttall's white-crowned sparrow (<i>Zonotrichia leucophrys nuttalli</i>)	2.23	1.80	1.57	38
Gambel's white-crowned sparrow (<i>Zonotrichia leucophrys gambelii</i>)	1.73	nm	nm	41
Dark-eyed junco (<i>Junco hyemalis</i>)	1.61	1.36	1.40	42

^aNote that all species that have been studied in the field are from the family Emberizidae. Kirn *et al.*⁴³ studied red-winged blackbirds (*Agelaius phoeniceus*), but with equivocal results.

^bNumbers represent ratios of song nucleus breeding volume to non-breeding volume.

Abbreviations: nm, not measured; RA, robust nucleus of the archistriatum.

ported anterogradely to RA and area X (Ref. 58). Exogenous BDNF decreases deafferentation-induced apoptosis in the RA of developing male zebra finches⁵⁹, and might be one trans-synaptic trophic factor that supports RA development in juveniles. If adult plasticity in the brain is mediated by similar processes to those that regulate development, then BDNF might be one component of the trans-synaptic support that HVC provides to RA and area X in adults.

Neuron number changes seasonally in HVC

Seasonal changes in the morphology of HVC were first demonstrated in male canaries by Nottebohm. He used Nissl-stained tissue to show that HVC volume³ and neuron number⁶⁰ were twice as large during the spring than during autumn (Table 3). The reliability of Nissl criteria to define the borders of song nuclei, especially HVC, was subsequently called into question (see Box 1). A wide series of studies have since shown, however, that the Nissl-defined borders of HVC coincide with those defined by a variety of other cytological markers, indicating that the volume and number of neurons in HVC do in fact change with season in several different species^{37,39,44,49,61,62}. In one study of wild song sparrows (*Melospiza melodia morphna*), for example, the number of neurons in HVC increased from approximately 150 000 in the late autumn to 250 000 in the early spring³⁷. This result was confirmed in this same species using a neuron-specific antibody to label and count HVC neurons⁶³. The seasonal volumetric growth of HVC clearly reflects seasonal neuronal addition into this nucleus.

This vernal increase in neuron number is a result of ongoing neurogenesis in the songbird brain^{64–67}. The adult HVC continues to incorporate new RA-projecting neurons and interneurons that replace older dying cells^{68,69}. This neuronal turnover is seasonally regulated and is greatest during the non-breeding season^{63,70}. Elevated circulating sex steroids appear to decrease the turnover and increase the survival of HVC neurons, thus increasing their numbers during the breeding season^{63,71,72}.

Seasonal changes in HVC neuronal turnover are correlated with changes in song behavior. Canaries learn to produce new song elements as adults and are therefore referred to as 'open-ended' or 'age-independent' song

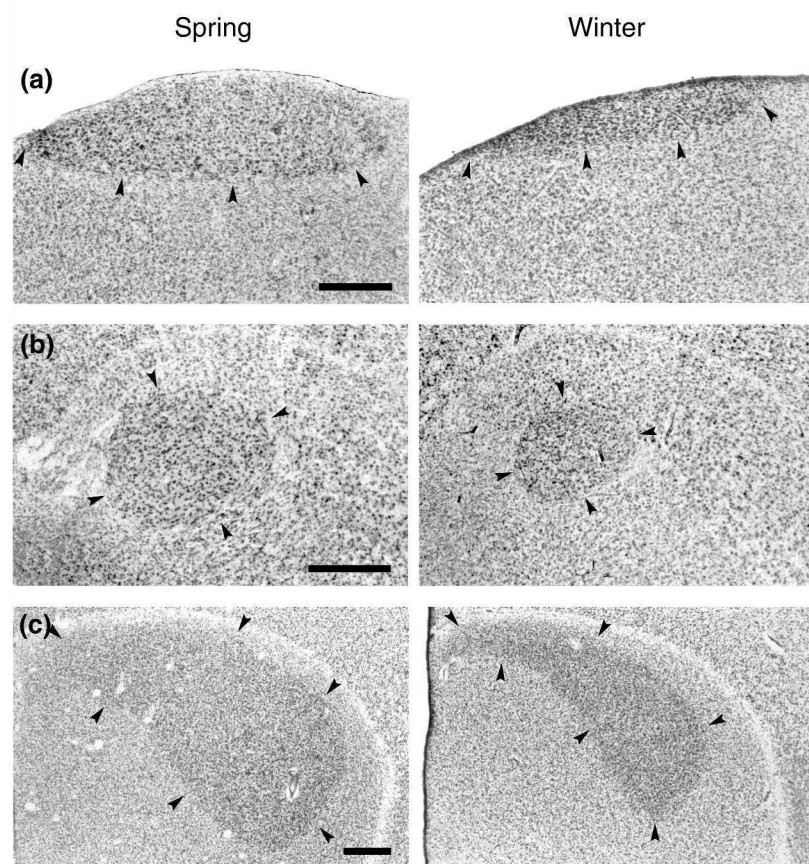


Fig. 2. Seasonal volumetric changes in the songbird brain. Wild male spotted towhees were collected and killed during the spring breeding season (left) and during the winter non-breeding season (right). Nissl-stained coronal sections through HVC (a), robust nucleus of the archistriatum (RA) (b) and area X (c) are shown. The overlying hippocampal formation has been removed in (a). Scale bars, 0.5 mm. Modified, with permission, from Ref. 40.

learners³⁶. Song learning in these birds occurs preferentially during the non-breeding season when song syllables are produced with less temporal and spectral stereotypy. These peak periods of song learning coincide with peaks in HVC neuronal recruitment⁷⁰, suggesting that perhaps seasonal patterns of neuronal replacement in HVC provide the neural substrate for seasonal song learning in adult birds^{65,70,73,74}. Recently, however, seasonally variable neuronal incorporation has also been demonstrated in adult song sparrows in which, as for canaries, HVC recruits more new neurons during the non-breeding season⁶³. Song sparrows are similar to canaries in that song stereotypy is diminished during

the non-breeding season³⁷. Unlike canaries, however, song sparrows are ‘critical-period’ or ‘age-limited’ learners and do not learn to produce new songs as adults. This observation suggests that seasonal patterns of neuronal turnover in HVC might be necessary, but not sufficient for adult song learning. Alternatively, perhaps seasonal patterns of neuronal turnover in HVC are more directly associated with seasonal changes in song stereotypy.

Dendritic growth and synaptogenesis in RA

The cellular basis of the volumetric growth of RA differs from that observed in HVC. Neuron number does not change seasonally in RA, but neuron size and spacing in this nucleus are both greater during the breeding season^{37,39,44,49,61,62,75}. The increase in neuronal spacing is associated with a vernal increase in the dendritic arborizations of RA neurons⁶⁰. Synaptic morphology also varies seasonally in RA, such that the sizes of presynaptic and postsynaptic profiles are largest during the breeding season in canaries⁷⁶. The number of transmitter vesicles per synapse is also greatest during the breeding season. In captive red-winged blackbirds (*Agelaius phoeniceus*), the density of dendritic spines on RA neurons was greater in males maintained on long, spring-like day lengths than in males on short days⁷⁷. These seasonal patterns of dendritic change suggest that synaptic efficacy in RA is enhanced during the breeding season⁷⁸. Electrophysiological studies should address this hypothesis.

Testosterone mediates seasonal changes in the song system

Several lines of evidence strongly suggest that testosterone (or its active metabolites) is the primary physiological cue that mediates the cyclical anatomical changes in the song circuitry. Several song nuclei, including HVC, RA, the medial and lateral portions of the magnocellular nucleus of the anterior neostriatum (mMAN and lMAN), the tracheosyringeal portion of the hypoglossal nucleus (nXIIts), and the dorsolateral nucleus of the medial thalamus (DLM) contain gonadal steroid receptors^{79–83}. The seasonal pattern of circulating testosterone correlates positively with the seasonal growth pattern of the song control circuitry^{3,37,38,40,41,63}. Castration strongly attenuates the seasonal growth of the song nuclei^{42,44,46}. Exogenous testosterone can induce song-nucleus growth in castrated males and non-breeding males in fall and winter^{44,71,75,84,85}.

TABLE 3. Experimentally induced plasticity of song control nuclei in captive male songbirds

Species	Treatment	HVC ^a	RA ^a	Area X ^a	Ref.
Canary (<i>Serinus canarius</i>)	Natural photoperiod April versus September	1.99	1.77	nm	3
Red-winged blackbird (<i>Agelaius phoeniceus</i>)	15 h versus 9.5 h light	1.34	1.28	1.42	43
Orange bishop (<i>Euplectes franciscanus</i>)	14 h versus 10 h light	1.80	1.60	nm	48
Eastern towhee (<i>Pipilo erythrophthalmus</i>)	15 h versus 9 h light	1.68	1.54	1.62	49
Gambel's white-crowned sparrow (<i>Zonotrichia leucophrys gambelii</i>)	20 h light and testosterone versus 8 h light ^b	1.82	1.71	1.57	44
European starling (<i>Sturnus vulgaris</i>)	P-stim versus P-refrac ^c	1.44	no change	no change	50
American tree sparrow (<i>Spizella arborea</i>)	20 h versus 8 h light	1.76	1.46	1.74	46

^aNumbers represent song nucleus volume ratios between treatment groups.

^bAll birds were castrated.

^cPhotostimulated (P-stim) males had testes that were not fully recrudesced (birds might not have been fully stimulated). After six to eight weeks of long days, males became photorefractory (P-refrac) and had fully regressed testes.

Abbreviations: nm, not measured; RA, robust nucleus of the archistriatum.

Box I. Reliable anatomical markers of song control nuclei

Most investigations of seasonal plasticity in the song system have used Nissl stains to visualize the borders of song nuclei. The reliability of these stains in this context was questioned by Gahr^{a,b}. He reported that the Nissl-defined borders of HVC were larger in breeding than in non-breeding male canaries, but that the size of this nucleus did not differ between these groups when measured by estrogen-receptor immunoreactivity. Gahr also reported that area X-projecting neurons lay outside the apparent Nissl-defined borders of HVC in non-breeding birds. Since Gahr's report, several investigators from different laboratories have compared seasonal volumetric changes of HVC using a Nissl stain and additional histological markers. All of these studies failed to replicate Gahr's observation and found that the Nissl-defined volume of HVC coincided with the volume as defined by other markers, regardless of season or hormone condition (see Table I). These studies demonstrate that the seasonal changes observed in the song nuclei using Nissl-stained tissue represent real changes in the structure of these regions. For a detailed discussion of this issue see Refs f,g,j.

TABLE I. Studies that have reported seasonal or hormonally induced changes in HVC volume using multiple histological markers

Species	Histological markers used	Refs
Canary (<i>Serinus canarius</i>)	Nissl stain, [³ H]DHT and E ₂ accumulation, RA- and area X-projecting neurons.	c,d,e
European starling (<i>Sturnus vulgaris</i>)	Nissl stain, α ₂ -adrenoceptor autoradiography.	f
Gambel's white-crowned sparrow (<i>Zonotrichia leucophrys gambelii</i>)	Nissl stain, area X-projecting neurons, acetylcholinesterase histochemistry.	g
Gambel's white-crowned sparrow (<i>Zonotrichia leucophrys gambelii</i>)	Nissl stain, androgen-receptor immunocytochemistry.	h
Western song sparrow (<i>Melospiza melodia morphna</i>)	Nissl stain, Hu immunocytochemistry.	i

Abbreviations: DHT, dihydrotestosterone; E₂, estradiol; RA, robust nucleus of the archistriatum.

References

- a Gahr, M. (1990) Delineation of a brain nucleus: comparisons of cytochemical, hodological, and cytoarchitectural views of the song control nucleus HVC of the adult canary. *J. Comp. Neurol.* 294, 30–36
- b Gahr, M. (1997) How should brain nuclei be delineated? Consequences for developmental mechanisms and for correlations of area size, neuron numbers and functions of brain nuclei. *Trends Neurosci.* 20, 58–62
- c Johnson, F. and Bottjer, S.W. (1993) Hormone-induced changes in identified cell populations of the higher vocal center in male canaries. *J. Neurobiol.* 24, 400–418
- d Rasika, S. *et al.* (1994) Testosterone increases the recruitment and/or survival of new high vocal center neurons in adult female canaries. *Proc. Natl. Acad. Sci. U. S. A.* 91, 7854–7858
- e Johnson, F. and Bottjer, S.W. (1995) Differential estrogen accumulation among populations of projection neurons in the higher vocal center of male canaries. *J. Neurobiol.* 26, 87–108
- f Bernard, D.J. and Ball, G.F. (1995) Two histological markers reveal a similar photoperiodic difference in the volume of the high vocal center in male European starlings. *J. Comp. Neurol.* 360, 726–734
- g Smith, G.T. *et al.* (1997) Seasonal changes in the size of the avian song control nucleus HVC defined by multiple histological markers. *J. Comp. Neurol.* 381, 253–261
- h Soma, K.K. *et al.* (1999) Seasonal changes in androgen receptor immunoreactivity in the song nucleus HVC of a wild bird. *J. Comp. Neurol.* 409, 224–236
- i Tramontin, A.D. and Brenowitz, E.A. (1999) A field study of seasonal neuronal incorporation into the song control system of a songbird that lacks adult song learning. *J. Neurobiol.* 40, 316–326
- j Brenowitz, E.A. (1997) Comparative approaches to the avian song system. *J. Neurobiol.* 33, 517–531

The effects of testosterone on HVC neuronal survival and the volumetric growth of this nucleus appear to be mediated (at least in part) through BDNF. Treatment with testosterone increases protein synthesis⁸⁶ and BDNF-like immunoreactivity in HVC (Ref. 87). Intraparenchymal BDNF infusion adjacent to HVC mimics the effects of testosterone, enhancing neuronal survival in HVC and increasing its volume. Finally, and most interestingly, neutralizing antibodies to BDNF block the effects of testosterone on neuronal survival within HVC and the volumetric growth of HVC. Insulin-like growth factors 1 and 2 have also been identified in the adult HVC (Refs 88,89). It will be informative to determine whether these factors also influence sex steroid action within HVC (Ref. 66).

Circulating testosterone can be converted to active androgenic and estrogenic metabolites in the brain⁹⁰. The enzyme 5α-reductase converts testosterone into 5α-dihydrotestosterone (DHT), and aromatase converts testosterone to estradiol (E₂). Furthermore, 5β-reductase is thought to inactivate testosterone by converting it to 5β-DHT. All of these enzymes are widely distributed in the songbird brain, thus, the effects of testosterone on the song system might be mediated through its conversion to one or more of these metabolites. In support of this hypothesis, exogenous 5α-DHT and E₂ delivered in combination can induce dendritic growth in the canary RA that is similar to that induced by testosterone treatment⁹¹. Note that exposure to either 5α-DHT or E₂ alone evokes less dendritic growth, perhaps suggesting some synergy between these metabolites. Additionally, E₂ pro-

motes the survival and decreases neuronal turnover in the canary HVC (Ref. 72). Apart from these studies, the possible roles of 5α-DHT and E₂ in the adult song system have received little attention.

Emerging evidence suggests that the sensitivity of the song nuclei to circulating testosterone might vary seasonally. At the end of the breeding season birds become refractory to the stimulatory effects of long days and the testes regress, sex steroid levels decrease in the blood and feather molt ensues⁹². During this photorefractory period, androgen- and estrogen-receptor production in HVC appear to be diminished^{41,93} (Fig. 3). One study has demonstrated that 5β-reductase levels in the hyperstriatum increase with the onset of photorefractoriness

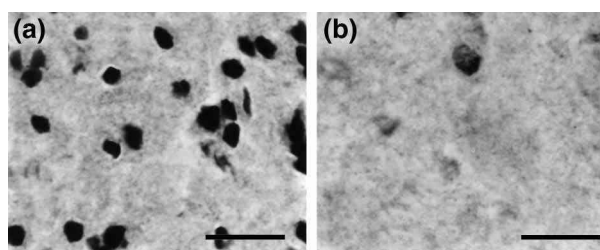


Fig. 3. Androgen-receptor immunoreactivity in HVC of wild white-crowned sparrows. Male birds were collected and killed during the spring breeding season (a) and during the autumnal migration (b). Immunolabel is localized to HVC cell nuclei and is more intense in breeding birds than in photorefractory birds. The density of immunopositive HVC cells is also greater in breeding birds. Scale bar, 20 μm. Modified, with permission, from Ref. 41.

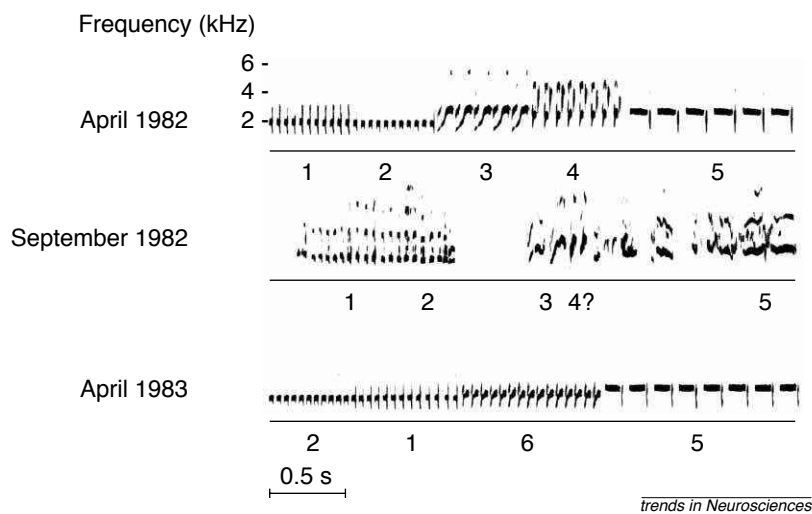


Fig. 4. Song stereotypy changes seasonally. Spectrograms are presented of songs recorded from a single adult male canary during two successive breeding seasons (April 1982 and 1983) and the intervening non-breeding season (September 1982). During April 1982, this bird's repertoire contained 28 highly stereotyped syllables (only five are shown). In September, song stereotypy was markedly decreased. For example, syllable 5 was produced as two simultaneous and independently modulated sounds. Canaries can learn new song elements as adults, and do so preferentially during such periods of song instability. By the following April (1983), this bird's song repertoire contained 35 syllables and song production was once again stable and stereotyped. Modified, with permission, from Ref. 36.

in European starlings (*Sturnus vulgaris*)⁹⁴, perhaps indicating that testosterone inactivation is enhanced in the brains of photorefractory birds. In another study, Bernard and Ball implanted photorefractory starlings with exogenous testosterone and reported no increase in HVC volume⁸⁵.

Non-steroidal cues contribute to seasonal plasticity

The seasonal plasticity in the song control system is not governed solely by gonadal steroids. Studies from two laboratories have indicated that manipulations of day length can induce changes in the song nuclei of castrated animals. Long days increased the volume of HVC slightly in castrated white-crowned sparrows⁴⁴ and starlings⁹⁵. Another study suggested that photostimulation increased the volumes of HVC, RA and area X in castrated American tree sparrows (*Spizella arborea*)⁴⁶. These researchers all pointed out that the gonad-independent effects of photoperiod were much less pronounced than those observed in gonadally intact birds. The interpretation of results from these studies of castrated animals must be tempered by reports of non-gonadal sources of sex steroids⁹⁶.

Several non-steroidal endocrine signals have been identified as potential mediators of song system plasticity. Melatonin binding in HVC and RA is photoperiodically regulated in captive house sparrows (*Passer domesticus*)⁹⁷, and exogenous melatonin can inhibit photo-induced song system growth in castrated starlings⁹⁵. Preliminary evidence suggests that thyroid hormones might also influence seasonal plasticity in the song control system, especially considering their involvement in seasonal plasticity of the avian gonadotropin system^{98–100}.

Why does the structure of the song system change seasonally? An hypothesis

The sustained peak performance of a seasonally predictable behavioral task is often preceded by hypertrophy of the organs or tissues, that support that task¹⁰¹. For example, the size of the gonads and other reproductive

structures increases dramatically in preparation for the annual breeding season and these organs regress when the breeding season is terminated⁴⁷. Long-distance migration in birds is preceded by a host of physiological changes including elevated fat stores and increased flight muscle mass^{102,103}. Anticipatory changes such as these are stimulated by seasonal environmental cues and mediated by neural and endocrine signaling mechanisms. The maintenance of hypertrophied organ systems and tissues is thought to be energetically expensive and so these systems regress when peak performance is not required^{101,104}.

The principles of performance-associated hypertrophy might also pertain to the seasonal plasticity of the song control circuitry. This hypothesis predicts that song performance should be enhanced during the breeding season. This prediction is supported by data from canaries, white-crowned sparrows and song sparrows. In these species, males sing more stereotyped songs (less song-to-song variability) during the spring breeding season, and song production is more frequent (more sustained) at this time of the year^{36,37,39,61,105} (Fig. 4). During the non-breeding season, birds sing less frequently and with less stereotypy (more variability).

Another prediction of the performance-associated hypertrophy hypothesis is that the growth of the song nuclei should occur in anticipation of behavioral changes. This appeared to be true in a study of captive white-crowned sparrows where seasonal cues initiated rapid song system growth that preceded significant improvements in song stereotypy³⁹. This prediction merits further study and does not exclude the possibility that experiential factors might also influence song system growth in complex ways. For example, perhaps singing can provide behavioral feedback that modifies song system growth. This idea has not been directly tested.

A third prediction of the performance-associated hypertrophy hypothesis is that the energetic costs of maintaining a fully developed song system throughout the non-breeding season outweigh those associated with recrudescing the song system each spring. Currently, the relative metabolic costs of maintaining or rebuilding the song system each year are not known.

Concluding remarks and prospects for the future

Seasonal plasticity of the song system can serve as a model to address the following questions, which are of fundamental importance to the study of neural plasticity in general.

- What are the mechanisms that mediate hormone action in the adult brain? Does hormone metabolism contribute to adult brain changes? How does trans-synaptic support from afferent and efferent targets support or influence, hormone action in a given brain region?
- What growth factors and trophic agents influence adult brain plasticity? This question has already received much attention in non-avian models, but the song system can shed light on how these agents synergize with or mediate, the effects of circulating hormones.
- How are neuronal proliferation, incorporation and survival in the adult brain controlled? What is the behavioral consequence of seasonally regulated neuronal turnover?

- Do neurons possess different electrophysiological characteristics in different seasons? To what extent is neural processing (for example, synaptic efficacy) affected by seasonal anatomical and physiological changes in these brain regions?
- What is the functional relevance of brain changes in adults? What are the behavioral consequences? Does plasticity facilitate adult learning?
- What are the costs and benefits associated with the seasonal growth and regression of brain centers?

Adult brain plasticity is a common phenomenon across a wide variety of animal taxa, and is a rich topic of investigation with many questions yet unanswered. Future studies should take advantage of the great diversity of seasonally breeding animals that exhibit naturally occurring cyclical brain changes. Such a comparative approach is likely to uncover general principles that govern dynamic events in the adult brain. In addition, this approach will provide fundamental insights into the behavioral consequences of structural changes in the adult brain.

Selected references

- Altman, J. (1962) Are new neurons formed in the brains of adult animals? *Science* 135, 1127–1128
- Bennett, E.L. *et al.* (1964) Chemical and anatomical plasticity of brain. *Science* 146, 610–619
- Nottebohm, F. (1981) A brain for all seasons: cyclical anatomical changes in song control nuclei of the canary brain. *Science* 214, 1368–1370
- Wayne, N.L. *et al.* (1998) Seasonal fluctuations in the secretory response of neuroendocrine cells of *Aplysia californica* to inhibitors of protein kinase A and protein kinase C. *Gen. Comp. Endocrinol.* 109, 356–365
- Belkin, K.J. and Abrams, T.W. (1998) The effect of the neuropeptide FMRFamide on *Aplysia californica* siphon motoneurons involves multiple ionic currents that vary seasonally. *J. Exp. Biol.* 201, 2225–2234
- Lnenicka, G.A. and Zhao, Y.G. (1991) Seasonal differences in the physiology and morphology of crayfish motor terminals. *J. Neurobiol.* 22, 561–569
- Pasmanik, M. and Callard, G.V. (1988) A high abundance androgen receptor in goldfish brain: Characteristics and seasonal changes. *Endocrinology* 123, 1162–1171
- McNulty, J.A. (1982) Morphologic evidence for seasonal changes in the pineal organ of the goldfish, *Carassius auratus*: a quantitative study. *Reprod. Nutr. Dev.* 22, 1061–1072
- Takami, S. and Urano, A. (1984) The volume of the toad medial amygdala-anterior preoptic complex is sexually dimorphic and seasonally variable. *Neurosci. Lett.* 44, 253–258
- Wade, J. and Crews, D. (1991) The relationship between reproductive state and 'sexually' dimorphic brain areas in sexually reproducing and parthenogenetic whiptail lizards. *J. Comp. Neurol.* 309, 507–514
- Barnea, A. and Nottebohm, F. (1994) Seasonal recruitment of hippocampal neurons in adult free-ranging black-capped chickadees. *Proc. Natl. Acad. Sci. U. S. A.* 91, 11217–11221
- Smulders, T.V. *et al.* (1995) Seasonal variation in hippocampal volume in a food-storing bird, the black-capped chickadee. *J. Neurobiol.* 27, 15–25
- Parry, D.M. *et al.* (1997) Immunocytochemical localization of GnRH precursor in the hypothalamus of European starlings during sexual maturation and photorefractoriness. *J. Neuroendocrinol.* 9, 235–243
- Parry, D.M. and Goldsmith, A.R. (1993) Ultrastructural evidence for changes in synaptic input to the hypothalamic luteinizing hormone-releasing hormone neurons in photosensitive and photorefractory starlings. *J. Neuroendocrinol.* 5, 387–395
- Forger, N.G. and Breedlove, S.M. (1987) Seasonal variation in mammalian striated muscle mass and motoneuron morphology. *J. Neurobiol.* 18, 155–165
- Buijs, R. *et al.* (1986) Seasonal variation in vasopressin innervation in the brain of the European hamster (*Cricetus cricetus*). *Brain Res.* 371, 193–196
- Xiong, J.J. *et al.* (1997) Evidence for seasonal plasticity in the gonadotropin-releasing hormone (GnRH) system of the ewe: Changes in synaptic inputs onto GnRH neurons. *Endocrinology* 138, 1240–1250
- Lee, W. *et al.* (1995) Photoperiod affects the expression of neural cell adhesion molecule and polysialic acid in the hypothalamus of the Siberian hamster. *Brain Res.* 690, 64–72
- Huang, L. *et al.* (1998) Photoperiod regulates neuronal bromodeoxyuridine labeling in the brain of a seasonally breeding mammal. *J. Neurobiol.* 36, 410–420
- Hofman, M.A. and Swaab, D.F. (1992) Seasonal changes in the suprachiasmatic nucleus of man. *Neurosci. Lett.* 139, 257–260
- Catchpole, C.K. and Slater P.J.B. (1995) *Bird Song: Biological Themes and Variations*, Cambridge University Press
- Vicario, D.S. (1991) Neural mechanisms of vocal production in songbirds. *Curr. Opin. Neurobiol.* 1, 595–600
- Margoliash, D. (1997) Functional organization of forebrain pathways for song production and perception. *J. Neurobiol.* 33, 671–693
- Nottebohm, F. *et al.* (1976) Central control of song in the canary, *Serinus canarius*. *J. Comp. Neurol.* 165, 457–486
- Brenowitz, E.A. (1991) Altered perception of species-specific song by female birds after lesions of a forebrain nucleus. *Science* 251, 303–305
- Del Negro, C. *et al.* (1998) The selectivity of sexual responses to song displays: Effects of partial chemical lesion of the HVC in female canaries. *Behav. Brain Res.* 96, 151–159
- Doupe, A.J. (1997) Song- and order-selective neurons in the songbird anterior forebrain and their emergence during vocal development. *J. Neurosci.* 17, 1147–1167
- Bottjer, S.W. *et al.* (1984) Forebrain lesions disrupt development but not maintenance of song in passerine birds. *Science* 224, 901–903
- Sohrabji, F. *et al.* (1990) Selective impairment of song learning following lesions of a forebrain nucleus in the juvenile zebra finch. *Behav. Neural Biol.* 53, 51–63
- Scharff, C. and Nottebohm, F. (1991) A comparative study of the behavioral deficits following lesions of various parts of the zebra finch song system: implications for vocal learning. *J. Neurosci.* 11, 2896–2913
- Scharff, C. *et al.* (1998) Conspecific and heterospecific song discrimination in male zebra finches with lesions in the anterior forebrain pathway. *J. Neurobiol.* 36, 81–90
- Burt, J.M. *et al.* Lesions of the anterior forebrain song control pathway in female canaries affect song perception in an operant task. *J. Neurobiol.* (in press)
- Foster, E.F. *et al.* (1997) Axonal connections of the medial magnocellular nucleus of the anterior neostriatum in zebra finches. *J. Comp. Neurol.* 382, 364–381
- Vates, G.E. *et al.* (1997) Reafferent thalamo-'cortical' loops in the song system of oscine songbirds. *J. Comp. Neurol.* 380, 275–290
- Vates, G.E. *et al.* (1996) Auditory pathways of caudal telencephalon and their relation to the song system of adult male zebra finches. *J. Comp. Neurol.* 366, 613–642
- Nottebohm, F. *et al.* (1986) Developmental and seasonal changes in canary song and their relation to changes in the anatomy of song control nuclei. *Behav. Neural Biol.* 46, 445–471
- Smith, G.T. *et al.* (1997) Seasonal changes in testosterone, neural attributes of song control nuclei, and song structure in wild songbirds. *J. Neurosci.* 17, 6001–6010
- Brenowitz, E.A. *et al.* (1998) Seasonal plasticity of the song control system in wild Nuttall's white-crowned sparrows. *J. Neurobiol.* 34, 69–82
- Tramontin, A.D. *et al.* (2000) Breeding conditions induce rapid and sequential growth in adult avian song control circuits: a model of seasonal plasticity in the brain. *J. Neurosci.* 20, 854–861
- Smith, G.T. (1996) Seasonal plasticity in the song nuclei of wild rufous-sided towhees. *Brain Res.* 734, 79–85
- Soma, K.K. *et al.* (1999) Seasonal changes in androgen receptor immunoreactivity in the song nucleus HVC of a wild bird. *J. Comp. Neurol.* 409, 224–236
- Gulledge, C.C. and Deviche, P. (1997) Androgen control of vocal control region volumes in a wild migratory songbird (*Junco hyemalis*) is region and possibly age dependent. *J. Neurobiol.* 32, 391–402
- Kirn, J.R. *et al.* (1989) Song-related brain regions in the red-winged blackbird are affected by sex and season but not repertoire size. *J. Neurobiol.* 20, 139–163
- Smith, G.T. *et al.* (1997) Roles of photoperiod and testosterone in seasonal plasticity of the avian song control system. *J. Neurobiol.* 32, 426–442
- Tramontin, A.D. *et al.* (1998) Contributions of social cues and photoperiod to seasonal plasticity in the adult avian song control system. *J. Neurosci.* 19, 476–483
- Bernard, D.J. *et al.* (1997) Testis-dependent and -independent effects of photoperiod on volumes of song control nuclei in American tree sparrows (*Spizella arborea*). *Brain Res.* 760, 163–169
- Wingfield, J.C. and Kenagy, G.J. (1991) Natural regulation of reproductive cycles, in *Vertebrate Endocrinology: Fundamentals and Biomedical Implications* (Schreibman, M. and Jones, R.E., eds), Academic Press
- Arai, O. *et al.* (1989) Correlation between the size of song control nuclei and plumage color change in orange bishop birds. *Neurosci. Lett.* 98, 144–148

- 49 Brenowitz, E.A. *et al.* (1991) Seasonal changes in avian song nuclei without seasonal changes in song repertoire. *J. Neurosci.* 11, 1367–1374
- 50 Bernard, D.J. and Ball, G.F. (1995) Two histological markers reveal a similar photoperiodic difference in the volume of the high vocal center in male European starlings. *J. Comp. Neurol.* 360, 726–734
- 51 Ball, G.F. (1999) Neuroendocrine basis of seasonal changes in vocal behavior among songbirds, in *Neural Mechanisms of Communication* (Hauser, M. and Konishi, M., eds), MIT Press
- 52 Bottjer, S.W. *et al.* (1985) Ontogeny of brain nuclei controlling song learning and behavior in zebra finches. *J. Neurosci.* 5, 1556–1562
- 53 Ramón y Cajal, S. (1959) *Degeneration and Regeneration of the Nervous System*, Hafner
- 54 Zann, R.A. (1996) *The Zebra Finch: A Synthesis of Field and Laboratory Studies* (Oxford Ornithology Series No. 5), Oxford University Press
- 55 Brenowitz, E.A. and Lent, K. (1999) Seasonal growth of adult avian song nuclei requires afferent input. *Soc. Neurosci. Abstr.* 25, 864
- 56 Herrmann, K. and Arnold, A.P. (1991) Lesions of HVC block the developmental masculinizing effects of estradiol in the female zebra finch song system. *J. Neurobiol.* 22, 29–39
- 57 Akutagawa, E. and Konishi, M. (1994) Two separate areas of the brain differentially guide the development of a song control nucleus in the zebra finch. *Proc. Natl. Acad. Sci. U. S. A.* 91, 12413–12417
- 58 Akutagawa, E. and Konishi, M. (1998) Transient expression and transport of brain-derived neurotrophic factor in the male zebra finch's song system during vocal development. *Proc. Natl. Acad. Sci. U. S. A.* 95, 11429–11434
- 59 Johnson, F. *et al.* (1997) Neurotrophins suppress apoptosis induced by deafferentation of an avian motor-cortical region. *J. Neurosci.* 17, 2101–2111
- 60 Nottebohm, F. (1987) Plasticity in adult avian central nervous system: Possible relation between hormones, learning, and brain repair. In *Handbook of Physiology* (Plum, F., ed), Williams and Wilkins
- 61 Smith, G.T. *et al.* (1995) Seasonal changes in song nuclei and song behavior in Gambel's white-crowned sparrows. *J. Neurobiol.* 28, 114–125
- 62 Tramontin, A.D. *et al.* (1998) Seasonal plasticity and sexual dimorphism in the avian song control system: stereological measurement of neuron density and number. *J. Comp. Neurol.* 396, 186–192
- 63 Tramontin, A.D. and Brenowitz, E.A. (1999) A field study of seasonal neuronal incorporation into the song control system of a songbird that lacks adult song learning. *J. Neurobiol.* 40, 316–326
- 64 Goldman, S.A. and Nottebohm, F. (1983) Neuronal production, migration, and differentiation in a vocal control nucleus of the adult female canary brain. *Proc. Natl. Acad. Sci. U. S. A.* 80, 2390–2394
- 65 Alvarez-Buylla, A. and Kirn, J.R. (1997) Birth, migration, incorporation, and death of vocal control neurons in adult songbirds. *J. Neurobiol.* 33, 585–601
- 66 Goldman, S.A. (1998) Adult neurogenesis: from canaries to the clinic. *J. Neurobiol.* 36, 267–286
- 67 Goldman, S.A. and Luskin, M.B. (1998) Strategies utilized by migrating neurons of the postnatal vertebrate forebrain. *Trends Neurosci.* 21, 107–114
- 68 Paton, J.A. *et al.* (1985) Cells born in adult canary forebrain are local interneurons. *J. Neurosci.* 5, 3088–3093
- 69 Kirn, J.R. and Nottebohm, F. (1993) Direct evidence for loss and replacement of projection neurons in adult canary brain. *J. Neurosci.* 13, 1654–1663
- 70 Kirn, J. *et al.* (1994) Cell death and neuronal recruitment in the high vocal center of adult male canaries are temporally related to changes in song. *Proc. Natl. Acad. Sci. U. S. A.* 91, 7844–7848
- 71 Rasika, S. *et al.* (1994) Testosterone increases the recruitment and/or survival of new high vocal center neurons in adult female canaries. *Proc. Natl. Acad. Sci. U. S. A.* 91, 7854–7858
- 72 Hidalgo, A. *et al.* (1995) Estrogens and non-estrogenic ovarian influences combine to promote the recruitment and decrease the turnover of new neurons in the adult female canary brain. *J. Neurobiol.* 27, 470–487
- 73 Nottebohm, F. (1989) From bird song to neurogenesis. *Sci. Amer.* 260, 74–79
- 74 Alvarez-Buylla, A. (1992) Neurogenesis and plasticity in the CNS of adult birds. *Exp. Neurol.* 115, 110–114
- 75 Johnson, F. and Bottjer, S.W. (1993) Hormone-induced changes in identified cell populations of the higher vocal center in male canaries. *J. Neurobiol.* 24, 400–418
- 76 DeVoogd, T.J. *et al.* (1985) Synaptogenesis and changes in synaptic morphology related to acquisition of a new behavior. *Brain Res.* 329, 304–308
- 77 Hill, K.M. and DeVoogd, T.J. (1991) Altered daylength affects dendritic structure in a song-related brain region in red-winged blackbirds. *Behav. Neural Biol.* 56, 240–250
- 78 DeVoogd, T.J. (1991) Endocrine modulation of the development and adult function of the avian song system. *Psychoneuroendocrinology* 16, 41–66
- 79 Arnold, A.P. *et al.* (1976) Hormone concentrating cells in vocal control and other areas of the brain of the zebra finch (*Poephila guttata*). *J. Comp. Neurol.* 165, 487–511
- 80 Gahr, M. (1990) Delineation of a brain nucleus: comparisons of cytochemical, hodological, and cytoarchitectural views of the song control nucleus HVC of the adult canary. *J. Comp. Neurol.* 294, 30–36
- 81 Balthazart, J. *et al.* (1992) Immunocytochemical localization of androgen receptors in the male songbird and quail brain. *J. Comp. Neurol.* 317, 407–420
- 82 Brenowitz, E.A. and Arnold, A.P. (1992) Hormone accumulation in song regions of the canary brain. *J. Neurobiol.* 23, 871–880
- 83 Smith, G.T. *et al.* (1996) Use of PG-21 immunocytochemistry to detect androgen receptors in the songbird brain. *J. Histochem. Cytochem.* 44, 1075–1080
- 84 Nottebohm, F. (1980) Testosterone triggers growth of brain vocal control nuclei in adult female canaries. *Brain Res.* 189, 429–436
- 85 Bernard, D.J. and Ball, G.F. (1997) Photoperiodic condition modulates the effects of testosterone on song control nuclei volumes in male European starlings. *Gen. Comp. Endocrinol.* 105, 276–283
- 86 Konishi, M. and Akutagawa, E. (1981) Androgen increases protein synthesis within the avian brain vocal control system. *Brain Res.* 222, 442–446
- 87 Rasika, S. *et al.* (1999) BDNF mediates the effects of testosterone on the survival of new neurons in an adult brain. *Neuron* 22, 53–62
- 88 Holzenberger, M. *et al.* (1997) Selective expression of insulin-like growth factor II in the songbird brain. *J. Neurosci.* 17, 6974–6987
- 89 Jiang, J. *et al.* (1998) Insulin-like growth factor-1 is a radial cell-associated neurotrophin that promotes neuronal recruitment from the adult songbird edpendyma/subependyma. *J. Neurobiol.* 36, 1–15
- 90 Schlinger, B.A. (1997) Sex steroids and their actions on the birdsong system. *J. Neurobiol.* 33, 619–631
- 91 DeVoogd, T. and Nottebohm, F. (1981) Gonadal hormones induce dendritic growth in the adult avian brain. *Science* 214, 202–204
- 92 Nicholls, T.J. *et al.* (1988) Photorefractoriness in birds and comparison with mammals. *Phys. Rev.* 68, 133–171
- 93 Gahr, M. and Metzendorf, R. (1997) Distribution and dynamics in the expression of androgen and estrogen receptors in vocal control systems of songbirds. *Brain Res. Bull.* 44, 509–517
- 94 Bottoni, L. and Massa, R. (1981) Seasonal changes in testosterone metabolism in the pituitary gland and central nervous system of the European starling (*Sturnus vulgaris*). *Gen. Comp. Endocrinol.* 43, 532–536
- 95 Bentley, G.E. *et al.* (1999) Seasonal neuroplasticity in the songbird telencephalon: A role for melatonin. *Proc. Natl. Acad. Sci. U. S. A.* 96, 4674–4679
- 96 Schlinger, B.A. *et al.* (1999) Androgen synthesis in a songbird: a study of cyp17 (17 α -hydroxylase/C17,20-lyase) activity in the zebra finch. *Gen. Comp. Endocrinol.* 113, 46–58
- 97 Whitfield-Rucker, M.G. and Cassone, V.M. (1996) Melatonin binding in the house sparrow song control system: Sexual dimorphism and the effect of photoperiod. *Horm. Behav.* 30, 528–537
- 98 Bentley, G.E. *et al.* (1997) The effects of nerve growth factor and anti-nerve growth factor antibody on the neuroendocrine reproductive system in the European starling *Sturnus vulgaris*. *J. Comp. Physiol.* 181, 133–141
- 99 Tekumalla, P. and Kirn, J.R. (1997) Distribution of thyroid hormone receptors in the zebra finch song system. *Soc. Neurosci. Abstr.* 23, 61
- 100 Tekumalla, P. *et al.* (1998) Analysis of seasonal thyroid function in adult male canaries. *Soc. Neurosci. Abstr.* 24, 1296
- 101 Piersma, T. and Lindstrom, A. (1997) Rapid reversible changes in organ size as a component of adaptive behavior. *Trends Ecol. Evol.* 12, 134–138
- 102 Gaunt, A.S. *et al.* (1990) Rapid atrophy and hypertrophy of an avian flight muscle. *Auk* 107, 649–659
- 103 Weber, T.P. and Piersma, T. (1996) Basal metabolic rate and the mass of tissues differing in metabolic scope: migration-related covariation between individual knots *Calidris canutus*. *J. Avian Biol.* 27, 215–224
- 104 Jacobs, L.F. (1996) Sexual selection and the brain. *Trends Evol. Ecol.* 11, 82–86
- 105 Bernard, D.J. *et al.* (1996) Age- and behavior-related variation in volumes of song control nuclei in male European starlings. *J. Neurobiol.* 30, 329–339

Acknowledgements

The authors' research is supported by the Virginia Merrill Bloedel Hearing Research Center, grant MH53032 from the NIH, and grant DGE-9616736AM02 from the NSF.