How the Brain Controls Birdsong

Song control centers in canaries' brains wax and wane as the birds acquire, and then discard, their song repertoires

In nature, male canaries sing to attract mates. In the laboratory, their songs are proving just as fascinating—to researchers who are exploring the brain changes that underlie learning. As shown by work from the laboratory of Fernando Nottebohm at Rockefeller University, the regions of the canary brain that control the movements of the musculature involved in song are remarkably plastic—capable of change—even in adult birds. The brain regions grow while the birds are learning to sing and then shrink during the time of year when the birds are silent, discarding their old song repertoires before they begin to learn new songs.

What the Nottebohm group is finding about neuronal properties often runs counter to the prevailing view of how nerve cells behave. For example, their results imply that the learning of some motor skills in adulthood depends on the formation of completely new synapses (connections between nerve cells), not just modulation of the activities of a fixed set of preexisting synapses. Moreover, their latest work indicates that the formation of neurons may not be limited to very early life, as is generally thought, but may also occur in mature birds.

Such findings have obvious implications for research aimed at treating brain and spinal cord damage, still intractable medical problems for all practical purposes. Nottebohm views song learning in birds as a good model for studying the brain's potential for repair. At a recent symposium on The Chemical Aspects of Brain, Behavior, and Neural Plasticity,* he said, "One can learn a good deal about plastic processes in the adult brain by focusing on parts of the brain that have evolved for learning."

Nottebohm's interest in song learning dates back more than 15 years. "What really got me into this work," he says, "was an observation, which was purely accidental, made at the end of the 1960's." At that time he was studying the effects on birdsong of cutting the tracheosyringeal (TS) nerves, which innervate the muscles of the syrinx, the vocal organ of birds. When both the right and left TS nerves were severed, the birds often experienced respiratory distress, which was sometimes severe enough to kill them. Nottebohm thus decided to cut only one of the nerves at a time. As it turned out, severing the right TS nerve had little effect on birdsong, whereas interrupting the left one dramatically reduced or eliminated it.

This result suggested a parallel with brain lateralization, then considered to be an exclusively human property. Studies by several investigators had shown a division of labor in the human brain, with the left side having dominant control over some activities, such as speech and related verbal skills, and the right dominating others, such as spatial abilities.

In cutting the motor nerve to the syrinx musculature, Nottebohm was examining only a peripheral effect, however. He could not tell whether the left-sided dominance he was seeing was due to lateralization in the brain, although there was a hint that it might be. Both sides of the syrinx have equal potential for singing. If Nottebohm cut the left TS nerve within 2 weeks of the bird's hatching, the animal would develop almost normal song under the control of the right nerve. He explains, "One can think of the syrinx as two musical instruments instead of one. Each side has its own air supply, its own sound source, its own musculature, and its own innervation."

To pin down the role of the brain, Nottebohm first had to identify the brain centers that are needed for motor control of the syrinx. With his Rockefeller colleagues Christiana Leonard and Tegner Stokes, he eventually located two such centers. The first, the hyperstriatum ventrale, pars caudale (HVc) sends nerve projections to the second, the nucleus robustus archistrialis (RA), which in turn sends projections to the hypoglossal nucleus in the brainstem. The TS nerve is a branch of a nerve tract originating in the hypoglossus.

Here Nottebohm was in luck. The HVc and RA nuclei have well-defined boundaries, which makes them easy to identify and to measure or destroy. Birdsong itself is easy to quantify. So Nottebohm was relating an easy-to-measure behavior to well-defined brain centers.

Destruction of the HVc's on both sides of the brain produces an almost silent bird, although the animals still have the motivation to sing. They go through the motions but produce little sound. "It looks like a canary singing on television with the sound turned down," Nottebohm says.

The brain centers on the left side did prove to have the dominant control of song. Destruction of the right HVc alone has only minor effects, whereas when the left is destroyed the bird reverts to a rudimentary type of song, similar to that produced when it first learns to sing.

Song learning in canaries requires some 8 to 9 months of practice. The birds begin with subsong about 1½ months after they hatch, which is usually in April. When they are about 2 months of age, subsong blends into plastic song. During these early stages the sounds delivered are very variable and of low amplitude. The birds appear to sing gently to themselves, often with their eyes closed, "much as a child going to sleep indulges in babbling," says Nottebohm, noting that Charles Darwin likened the early song of birds to the babbling of human infants. Canaries do not produce full adult song until about January. They continue to sing for 6 to 7 months but become silent during late summer. Then, in the fall, they start singing again and develop a new song repertoire.

Adult birds with either right or left HVc lesions can learn new song repertoires in the next season, according to Nottebohm. This suggests that the right brain centers have the potential to control song but have a subordinate role as long as the centers on the left side are intact. Thus the canary brain normally has unused capacity plus the plasticity needed to transfer control of a learned behavior to the less used centers, reversing the normal pattern of hemispheric dominance.

Nottebohm has found that the size of song control nuclei is correlated with the size of the canaries' song repertoires. The nuclei are very small in newly hatched birds and grow during the song learning months. "Song learning is a very protracted affair. We are talking

*The symposium was held in Philadelphia on 3 and 4 June under the auspices of the Institute for Child Development Research.

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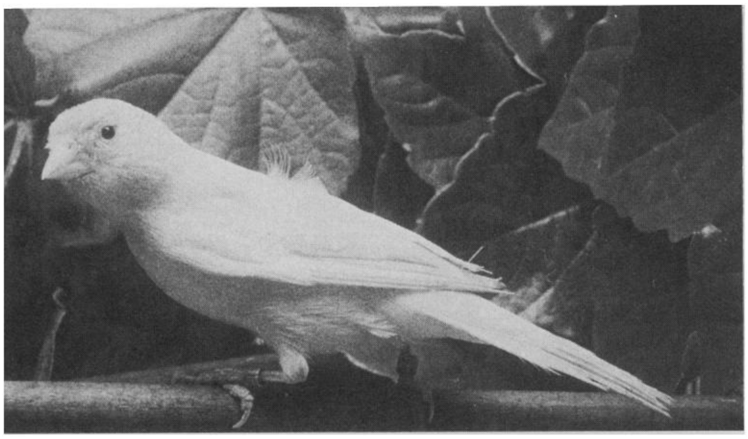

Fernando Nottebohm

Serinus canarius

Singing for science

about a long time during which anatomical changes can occur," Nottebohm points out. In his early studies the average sizes of the nuclei appeared to remain constant when they were measured each year in the spring, when the birds are in full song.

There was a great deal of size variation from bird to bird, however. Male birds with small centers generally have small song repertoires, whereas those with large nuclei often, but not always, have large vocabularies. Nottebohm explains this by analogy with a library: "You can have lots of shelves without lots of books, but if you want lots of books, you need lots of shelves." Surprisingly, in view of the normal dominance of the left song centers, no size differences are observed between the nuclei on the two sides of the brain. In contrast, there are often marked anatomic variations between comparable regions on the two sides of the human brain, which may be related to human brain lateralization.

Until last year, Nottebohm and his colleagues thought that the sizes of the HVc and RA remain constant after the canaries reach maturity. But this view was based on measurements made only during the spring. In a more recent study, he measured the nuclei in the spring and about 5 months later, at the end of the molt, in September. Much to his surprise, the song control nuclei were considerably smaller in the fall than in the spring. The average volumes of the whole brain and of two brain nuclei not involved in song control showed less marked seasonal differences.

These results indicate that the size of the song control nuclei increases during song learning but then decreases during the summer and early fall as the songs are discarded. "At the time when that year's song repertoire is being lost," Nottebohm says, "the birds are not only discarding the songs but are throwing away the part of the anatomy with which the song has been learned."

The Rockefeller workers are now trying to pin down the specific neural changes that accompany learning. Some clues come from their studies of the song control nuclei in female canaries. In accord with the view that the size of the nuclei is correlated with the size of the song repertoire, Nottebohm and Arthur Arnold, who is now at the University of California at Los Angeles, have found that the nuclei in the brains of the females, which sing very little, are about one-quarter as large as those of males.

Adult female canaries can be induced to sing by treating the ovariectomized birds with the male hormone testosterone, although the song repertoires they acquire are not as extensive or varied as those of males. During the hormone treatment, the size of the HVc and RA nuclei increases. Nottebohm remarks, "There is a very dramatic change in the anatomy of the adult brain under the influence of physiological levels of hormone at the time when new behavior is being acquired."

Testosterone works, at least in part, by increasing the length and degree of branching of the dendrites of some neurons in the brain centers. (Dendrites are neural projections that receive connections from other nerve cells.) According to Nottebohm and Timothy DeVoogd, who is currently at Cornell University, the dendritic volume of one class of RA neurons is about 1.7 times greater in adult males than in females. In ovariectomized females treated with testosterone, the size of the dendritic trees increases until it is the same as that in males. Nottebohm says, "This suggests that there might be a direct effect of the hormone on the genome, making for greater dendritic length." Arnold has shown that some HVc and RA nerve cells accumulate testosterone, possibly a preliminary to the hormone's action.

Nottebohm hypothesizes that the formation of new synapses is necessary for some kinds of learning. Preliminary evidence, obtained by Nottebohm in collaboration with DeVoogd and Barbara Nixsdorf of Rockefeller, suggests that the density of synapses on the dendrites does not change under the influence of testosterone, but the greater length of the projections would accommodate more connections. According to the hypothesis, the annual cycle of song learning and loss in males is accompanied by a growing and then shedding of synapses, "much in the way that trees grow leaves in the spring and shed them in the fall." Production of testosterone in the males decreases during their silent months and increases again as the mating—and singing—season approaches.

Nottebohm terms the shrinkage of dendrites and the consequent loss of synapses a "rejuvenation," causing a return of the canaries to an earlier developmental state. There is a caveat, however. The term applies only if a new wave of synapse formation follows. The question then arises whether a similar typse of rejuvenation might be induced to repair damage in a human brain.

Perhaps most surprising of all were the unpublished results of an experiment described by Nottebohm at the Philadelphia symposium. To test whether testosterone induces the formation of new neurons in addition to increasing dendrite length, Nottebohm and Steven Goldman of Rockefeller injected intact adult female canaries first with the hormone and then with radiolabeled thymidine, which is incorporated into the DNA of only newly formed cells. Two days after the thymidine injection, the label appeared in the cells on the outer layer of the HVc. Some 30 days later it could be seen in neurons within the nucleus. This may parallel the normal development of HVc neurons. The findings seem to suggest that testosterone stimulated neuronal proliferation. But it did not.

"What turned out to be the false lead," Nottebohm explains, "was the effect of testosterone in all this." Giving thymidine first and then testosterone produced exactly the same result. "The implication was that neuronal proliferation was going on at the time regardless of what we did."

Moreover, the neuronal recruitment appeared to be very active. The percent of cells labeled per day was so high that the volume of the HVc might double in as few as 47 days, Nottebohm says, without a corresponding neuron loss.

Formation of new neurons also seems to occur in HVc's of male canary brains. Nottebohm says, "It seems reasonable to suggest at this time that the recruitment of new neurons in the HVc nucleus of adult male and female canaries is likely to play an important role in the encoding and decoding of a learned vocal repertoire."—JEAN L. MARX