

no effect on the skeletal neuromuscular blockage. An oxime increases the effectiveness of drug therapy in poisoning by some, but not all, cholinesterase inhibitors. Unlike atropine, it acts by reactivating the inhibited enzyme at nicotinic as well as muscarinic sites and therefore relieves the skeletal neuromuscular block (2, 3). The guidance put out by the Department of Defense on the treatment of anticholinesterase poisoning stresses the fact that an oxime is to be used as an adjunct to atropine (4).

Also, we have found that the iodine salt is not the oxime of choice because of its comparatively low solubility in water and because of the possibility of producing iodism. The chloride salt (pralidoxime chloride) has been evaluated extensively and is the oxime of choice for use in combination with atropine (2).

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22 June 1970

My article discusses a basic problem of the molecular biology of excitable membranes. The casual remark referring to the existence of a highly efficient and successful antidote against intoxication by organophosphate insecticides (OPI) was prompted by the present interest in environmental control of pesticides and by the article in *The New Yorker* (1) describing the treatment of an accidental victim of OPI intoxication.

In contrast to atropine, which is toxic in milligram concentrations, pyridine 2-aldoxime methiodide (PAM) is harmless to humans at a concentration of 1 to 2 g. Oximes are widely accepted to be the antidote that repairs the specific biochemical lesion caused by OPI; they reverse the block of acetylcholinesterase, the basic cause of the fatal effects. Atropine helps by protecting the receptor protein against excess acetylcholine, one of the indirect effects of acetylcholinesterase block, but it does not

reverse the inactivation of the enzyme. We demonstrated that animals injected with 10- to 20-fold sure (100 percent) lethal doses of OPI survived when treated with PAM in combination with atropine (2). Also, a series of articles [see, for example, the paper by Namba and Hiraki (3)] have been published describing the success of PAM when applied to severe cases of OPI intoxication of agricultural workers. (In the commercial product, the iodine salt of PAM was replaced by the chloride many years ago.)

A recent article in *Science News* (4) about treatment of OPI poisoning refers to PAM as the "key antidote." Van Sint, the scientific director of the Army's Chemical Warfare Center, emphasizes the crucial role of PAM, whereas in his comment (5) Sim stresses the role of atropine and refers to PAM as an "adjunct" to atropine. The recent deaths caused by parathion (6) would most likely have been prevented if the

physicians had not used atropine alone as the antidote (according to the report), but had used PAM in conjunction with atropine. Although widely used in many other countries, PAM is surprisingly little known to physicians in this country. The article in *Science News* is most timely and fortunate, drawing attention to the lifesaving role of PAM instead of playing it down.

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4. *Science News* **98**, 137 (1970).
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6. J. N. Wilford, *The New York Times*, 21 August 1970.

23 September 1970

Lesch-Nyhan Syndrome: Preventive Control

Our paper "Lesch-Nyhan syndrome: Preventive control by prenatal diagnosis" (1) contained an error drawn to our attention by Dr. Walter E. Nance. The last two sentences should read:

"Thus the diagnosis of index cases is of practical, rather than theoretical, importance in that this information will lead to the identification of heterozygotic mothers who are at risk of bearing additional affected children and raises the need for examination of such mothers as well as other female relatives for evidence of cell mosaicism for the HGPRT enzyme. Theoretically, new mutations not reflected in the

mothers' somatic cells could account for as many as one-third of cases. However, mosaicism has been found in all of the ten mothers so far examined in this laboratory. This disease may now be added to the list of disorders detectable by prenatal diagnosis (13)."

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Reference

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Lateralization of Bird Song

Nottebohm (1) has recently published results of experiments in which the hypoglossal nerves serving the syrinx of chaffinches were sectioned unilaterally. When the left nerve was sectioned either of two results occurred, many song elements disappeared completely although a few remained, or alternatively, in place of the absent elements were new patterns which were interpreted as distortions of those formerly present. In contrast, when the right nerve was sectioned

alone only a few elements disappeared.

From these results Nottebohm then speculates on the lateralization of control of song within the central nervous system, and secondly, on the control of song through means independent of the need of proprioceptive feedback once development has terminated. This latter suggestion was made since some elements of the songs appear unchanged after sectioning. It is particularly this latter interpretation which I question.

It seems to me that there are three observations which do not receive adequate explanations from Nottebohm's account. Why is it that on unilateral sectioning only some portions of the songs disappear and not others? What is the basis for the alternative result of the appearance of highly modified sounds? Finally, why are there two alternatives?

A further examination of these questions might be achieved if we consider that there is ample evidence of lateralization within the effectors of sound. That is, the main sources of sound in birds are the internal tympaniform membranes, one associated with each bronchus (2). Although there is as yet no conclusive evidence that these particular sources can function independently, there is quite convincing evidence that two sources do so act in many species of song birds for members of these species can sing two separate tunes simultaneously [see (3)].

It seems reasonable therefore that the complex vocal patterns of chaffinch song may in some cases reflect the independent operation of the two sources. Hence, when motor input through the hypoglossal nerve is sectioned unilaterally, the operation may eliminate only one of the two sources. This would explain why only some sounds disappear on sectioning, the remainder being produced by the unaffected source. Also, if this interpretation is correct, then the left source seems to produce more elements of chaffinch song than the right.

From the foregoing we see that the constancy of sounds after unilateral sectioning of the hypoglossal nerve need not reflect the unimportance of proprioceptive feedback. In fact, the observation that some elements are replaced by others of less-controlled organization is precisely the kind of change one expects if essential feedback has been removed.

Our understanding of the nervous control of the syrinx is still so limited that many possibilities seem open. One of these is that alternative motor pathways to the syrinx may be used, especially after a normal route has been cut. Otherwise, if there are two sources of sound, how should one explain the production from the sectioned side of even distorted sounds?

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3. C. H. Greenewalt, *Bird Song: Acoustics and Physiology* (Smithsonian Institution Press, Washington, D.C., 1968).

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Lemon raises three questions, one concerning the anatomy of sound production, a second regarding the evidence for neural lateralization of vocal control, and a third having to do with the importance of proprioceptive feedback in the maintenance of song in adult chaffinches. I will answer them in that order. The observation of neural lateralization of vocal control in a song bird is so novel a phenomenon, and the underlying anatomy and physiology so unfamiliar to most readers, that I have devoted a separate publication to discuss those matters in considerable detail (1).

The internal tympaniform membrane in each bronchus acts as an independent sound source (2) with its own muscular and nervous control, the latter provided by a branch of the hypoglossus nerve. Unilateral section of this nerve removes control over the half of the syrinx it innervates. It seems probable that according to the extent of air flow through this denervated half, the internal tympaniform membrane may or may not vibrate and produce audible sound or not, which accounts for the fact that normal components of song may be replaced by silent gaps or by unrelated sounds. Rüppell (3) showed that the excised syrinx of a gull, placed in a pressure chamber, will generate sound as air flows through it in a cephalad direction. Miskimen (4) was able to elicit sound by forcing air in a cephalad direction through the syrinx of anesthetized house sparrows, ring-necked pheasants, and starlings. Thus, it is possible to separate to some extent the mechanism responsible for sound production from that one responsible for the modulation of complex song. In the chaffinch those components of song which survive unilateral denervation of the syrinx unaltered are presumably contributed by the intact half of the syrinx, whereas novel sounds replacing lost song components are contributed by the denervated half.

The syringeal innervation in the chaffinch was described 55 years ago (5). It is morphologically symmetrical so that each side of the syrinx receives

a hypoglossal branch and a much smaller one from the vagus. Ipsilateral section of the latter does not add to the effects of sectioning the right or left hypoglossus. No other motor pathways to the syrinx are known. I did control for nerve regrowth and rerouting of fibers by section of the hypoglossal roots and section of the vagus on that same side. Cutting the musculature of the denervated half of the syrinx does not add to the effects of unilateral denervation. Therefore, the persistence of intact song elements following unilateral denervation of the syrinx can only be attributed to hypoglossal control over the intact half of the syrinx. Similarly, the development of normal song by the intact "subordinate" side after denervation of the "dominant" one in young birds can only be explained by the previously subordinate half of the syrinx now contributing all components of song. These observations led me to invoke a neural lateralization of function with a dominant (left) and subordinate (right) hypoglossus controlling song production in the adult, although this can be reversed by injury before the onset of song.

Finally, it was the loss of some components of song following unilateral denervation of the syrinx while others are retained intact that led me to conclude that "song is not controlled by a dynamic relation between output and feedback involving the entirety of the song pattern," "entirety" being the key word here. The performance of deaf birds was no more hindered than that of hearing ones. This finding is as startling as if denervation of the right or left hand of a deaf pianist were found not to affect the nature and timing of the contributions of the intact hand. Neither bird nor pianist is allowed to read the music. Other observations on the song of a deaf adult chaffinch emphasize the importance of a central pattern. Several months after cutting both hypoglossal nerves, syringeal reinnervation will have occurred. However, the structure of song will be abnormal, presumably because of imperfect reinnervation of the syringeal muscles. Yet, such a bird renders different song themes with considerable stereotypy (1, 6).

Since auditory feedback was absent in this case and proprioceptive feedback was modified, here too it is tempting to attribute the stability of a song to the unaltered persistence of a

central output pattern. The possibility that a fully learned motor pattern may become independent of peripheral control is of considerable neurological interest. It will be difficult to test this conclusively in the case of chaffinch song since it would require the elimination of all relevant proprioception accompanying song production.

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References and Notes

1. S. J. McNaughton and L. L. Wolf, *Science* 167, 131 (1970).
2. The index is of the form:
$$W = \left[\frac{\sum (y_p \cdot p^2) - (\sum y_p \cdot p)^2 / \sum y_p}{\sum y_p} \right]^{1/2}$$
where p is the position of the community ordered on an environmental gradient from 1 to 10, y_p is the importance of the species in that community, $\sum y_p$ is the total importance of the species for all its occurrences, and W is an index of niche width of the species [Erratum, *Science* 168, 455 (1970)].
3. B. Maguire, Jr., *Amer. Natur.* 101, 515 (1967).
4. K. Fujii, *Syst. Zool.* 18, 151 (1969).
5. I thank an anonymous reviewer for his comments.

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Community Ordering and Niche Width

McNaughton and Wolf (1) proposed an index of niche width based upon both the importance and position of species along one-dimensional environmental gradients. A simple example illustrates a possible danger in using this technique in certain environmental orderings.

In community ordination, the performance of such elementary operations as multiplication and addition requires that mapping numbers (for example, values for the position of a community in an environmental ordering running from 1 to 10) are isomorphic to some numerical structure which includes these operations. When communities are ranked with numerical scores and these scores are manipulated by addition and division [as is the case for the McNaughton and Wolf index (2)], then it is assumed that the ranking technique is isomorphic to arithmetic. Since community ordination is usually not isomorphic with arithmetic, different ordination techniques can produce very different indices of niche width.

For example, assume that an investigator has ordered a secondary successional gradient by ranking ten communities from 1 to 10 according to their differences and that the communities are evenly spaced along this ordination. Two hypothetical species, A and B, occur in the different communities such that A has an importance of 36 in community 1 and an importance of 1 in communities 2, 3, 4, and 5, and B has an importance of 36 in community 10 and an importance of 1 in communities 6, 7, 8, and 9. Importance can refer to such measures as biomass, density, summated home range (for animals), or coverage (for plants). With the McNaughton and Wolf index, the niche width (W) for these two species is the same under this ordination scheme ($W = .8291$). However, let us

further assume that the investigator notes that community 1 occurs after 10 years of succession, that community 10 occurs after 100 years, and that each of the other communities occurs after the respective ordinal rank of the community squared plus 10 years. Thus, by dividing the age of the community by 10 a new ordination with ranks running from 1 to 10 can be devised. With the new ordination ranks for the communities, the niche width of species B ($W = 1.1103$) is more than twice that of species A ($W = .4759$).

Since the niche width formula given by McNaughton and Wolf (1) weights the importance of the species according to their positions in the environmental gradient, one can easily see from the above example that the parameter used for ordering should not be arbitrary. Niche-width indices (W 's) based upon ordinations of community ages, differences, temperatures, altitudes, amounts of moisture, and other ecological factors can differ in both magnitude and proportion. Selecting one ordination technique from the virtually infinite set of possible techniques is almost by necessity arbitrary.

If one uses positions along a community ordination to ascertain niche width, he should be certain that his niche-width index does not require the ordination to be isomorphic to arithmetic. One such index has been used for protozoa (3). An alternative is to use individual- or population-level data in conjunction with statistical techniques currently common in numerical taxonomy, thus circumventing the need for any community ordination (4).

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In his comment on our discussion of niche width (1), Shugart correctly points out a possible difficulty in using our index (2). An important question that arises is whether environmental ranges should be subdivided arbitrarily for the purposes of niche-width calculation or according to characteristics of the organisms involved. A major conclusion of our article was that different species tend to specialize on different environmental parameters, thus making it highly unlikely that one can divide any environmental gradient symmetrically for all species. Shugart's example converts communities 1 to 5 to 1 to 3.5 and 6 to 10 to 4.6 to 10 or vice versa, depending upon which ordination is most appropriate. We assume that few ecologists would, as Shugart suggests, arbitrarily order a successional sequence by 10-year intervals since succession is obviously nonlinear on time. The problem of asymmetry in ordination has been so thoroughly discussed (3) that we felt ecologists employing our index would be aware of pitfalls of the type pointed out by Shugart. With the data available to us, more refined techniques seemed unnecessary and unwarranted. Other niche-width indices may be found preferable as more data become available for the definition of niche parameters. As we said in our introduction, "it is hoped that we will stimulate tests of the relevance of the model proposed to such carefully defined niches."

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22 October 1970