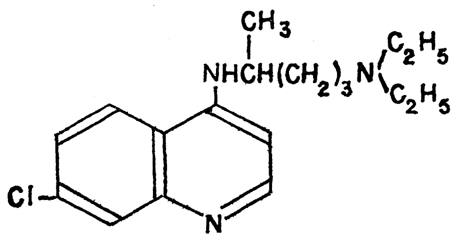

Chloroquine

Fig. 4. Structure of chloroquine; the compound has a molecular weight of 319.9.

is specifically involved in the binding of chloroquine to DNA (*10*).

Kurnick and Radcliffe have observed an enhancement of the viscosity of DNA solutions by chloroquine (*9*); this suggests to us that the drug forms a complex with DNA in a manner which resembles the interaction of DNA with mepacrine (Atebrin) (*16*).

The two nonheterocyclic amino groups of chloroquine (Fig. 4) are separated by four carbon atoms: the drug may be considered a substituted 1,4-diaminopentane. Among primary aliphatic diamines of graded chain lengths, diaminobutane and -pentane are strongest in elevating the T_m of DNA (*17*) although concentrations of the range of $10^{-3}M$ are required to produce effects comparable to those of $10^{-5}M$ chloroquine. Spermine, on the other hand, which possesses two secondary amino groups separated by four carbon atoms, is as active as chloroquine at equivalent molar concentrations in elevating the T_m of DNA (*18*). We are proposing that nonprimary diaminobutanes stabilize the DNA helix by ionic interaction with phosphoric acid groups. The electronegatively substituted heterocyclic systems of chloroquine and mepacrine may contribute additionally to the formation of complexes with DNA.

The actions of these and other chemotherapeutic agents upon DNA may offer an opportunity to probe the DNA molecule for specific structural features that are essential for the replication of DNA or for the transcription of RNA.

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15 June 1965

Color-Discrimination Performance of Pigeons: Effects of Reward

Abstract. *Performance of two pigeons given tasks in discriminating colors was examined on trials before and after they had occasionally received rewards for pecking when exposed to light of specific wavelengths. After a reward, the probability that the birds would respond to light stimuli that were never rewarded was higher than before the reward was given, but paradoxically the birds showed no general decline in their ability to differentiate between stimuli at wavelengths 1 millimicron apart.*

Reward plays an important role in several behavioral phenomena; responses maintained by reward cease if the reward is not made available. During discrimination tests in which responses to one stimulus are sometimes rewarded while responses to a second stimulus are never rewarded, the subject tends to respond to the rewarded stimulus with a higher probability or a faster rate. We have noted, however, that performance in discrimination is relatively poorer after a reward has been given than before; for a short time there is an increased tendency for the subject to respond to the stimulus not associated with reward, which decreases the difference in relative probability of response to the two stimuli.

Thus, in contrast with its long-range salutary effect on performance in discrimination, the short-range effect of a reward may be thought to be interference with discrimination; unrewarded stimuli elicit responses more frequently, a situation sometimes called loss of stimulus control. The exact nature of the decline in performance has not been studied.

We have analyzed much data on performance in discrimination, derived from two birds that were trained on a problem of spectral discrimination for more than 1000 hours. The birds were presented with a random sequence of monochromatic light values, closely spaced physically, in an otherwise darkened chamber. To each exposure they could respond by pecking a 2.5-cm circular key on which the light was projected for 2 seconds. Occasionally the pigeon was rewarded by the brief availability of grain if it pecked in response to certain of the wavelengths, never if it pecked in response to other wavelengths. After a peck and between trials the key was darkened for a variable period averaging 2 seconds from the end of each trial.

The two birds worked on different problems. One was presented with the ten wavelengths from 530 to 539 mμ at 1-mμ intervals and was occasionally rewarded for responding to the upper five values, 535 to 539 mμ. The second bird was rewarded only for responding to 535 mμ, the middle value of the 11 wavelengths evenly spaced between 530 and 540 mμ, inclusive. The data cover various probabilities of occurrence of the several stimuli, probabilities of reward (typically 2 or 3 times per 100 trials), and durations of rewards. Since the effects of all such manipulations proved to be virtually independent of the effects reported here, we pooled all data for the following analysis.

A LINC computer operating on-line provided all the control and recording functions. During the latter portion of the discrimination training, the schedule of stimuli and information on response were recorded and stored separately for each trial, so that the results of some 100,000 trials were available for each bird.

Analysis of the data by the computer located every trial on which a reward was available and during which a peck occurred (presumably the bird

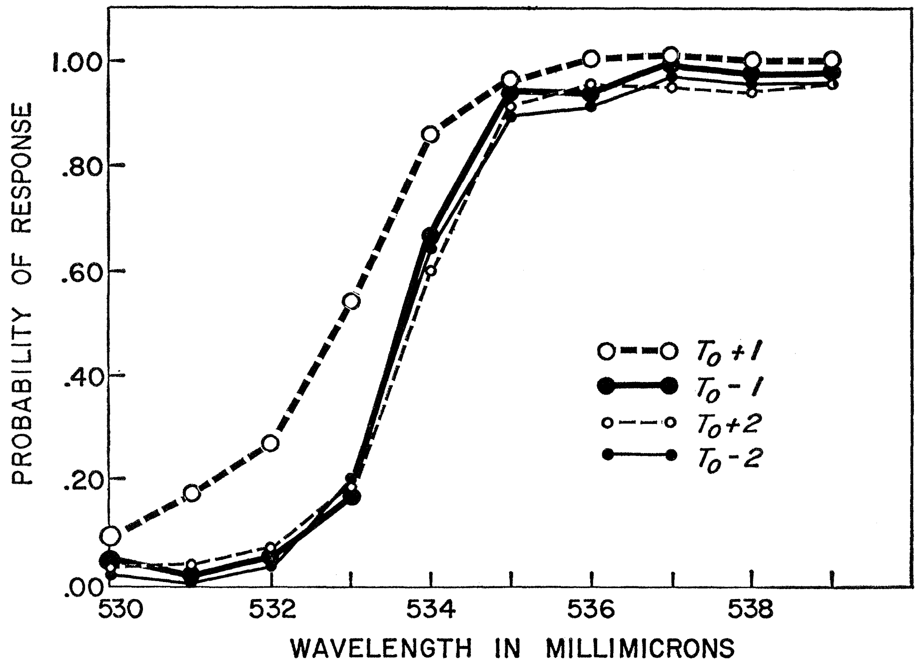

Fig. 1. Probability of response by a pigeon to light of various wavelengths on four trials preceding ($T_0 - 2$, $T_0 - 1$) and following ($T_0 + 1$, $T_0 + 2$) the trial (T_0) on which a reward was given. This bird was occasionally rewarded for pecking in response to 535 through 539 mμ.

was rewarded). The number of times each stimulus appeared and the number of trials on which pecks occurred before and after rewarded trials were then tabulated separately.

The effect of reward on performance can be demonstrated by comparing performance on the trial immediately preceding reward with that on the trial immediately following reward. Such data appear in Figs. 1 (based on 1500 pecks by one bird) and 2 (based on 1000 pecks by the other). In both figures, the trial preceding reward is a heavy solid line; the trial immediately following reward is a heavy dashed line. Both pigeons performed remarkably in discrimination, with a pronounced after-reward effect in which there was a higher probability of response to all unrewarded stimuli. Figure 1 shows the performance of the bird rewarded for responses to the wavelengths 535 through 539 mμ; Fig. 2, the bird rewarded only for responses to 535 mμ.

The stability of the data is attested to by the close correspondence between the curves for the last and second-to-the-last trials preceding the rewarded pecks, $T_0 - 1$ and $T_0 - 2$. The effort of the reward virtually disappeared by the second trial after the reward ($T_0 + 2$), perhaps less so for the bird in Fig. 2.

Clearly there is a tendency after a reward to respond more often to stimuli not entailing a reward. If the stimuli were somehow less important as governors of behavior after a reward, the result should be a decrease in the slopes of the curves. Our data indicate, however, that the birds, at least for some pairs of wavelengths only 1 nm apart, differentiated as well or almost as well after a reward as before. This does not seem to be a reduction of the degree to which stimuli control behavior. There was no marked decrease after reward in ability of the pigeon to respond differentially to closely spaced wavelengths. We can only describe the effect somewhat inexactly as a change in response bias.

The impact of the effect is apparent only because we obtained data at several points; had we used only one rewarded and one nonrewarded stimulus the result would probably have appeared to be only a relatively greater probability of response to the nonrewarded stimulus after receipt of a reward. As to the general problem of the relation between reward and discrimination performance, there may be local, short-lived consequences of reward that are inimical to effective performance in discrimination; such effects, however, seem unrelated to ability to discriminate. The question of whether these effects also occur early in training or only after considerable experience on a problem in discrimination remains open.

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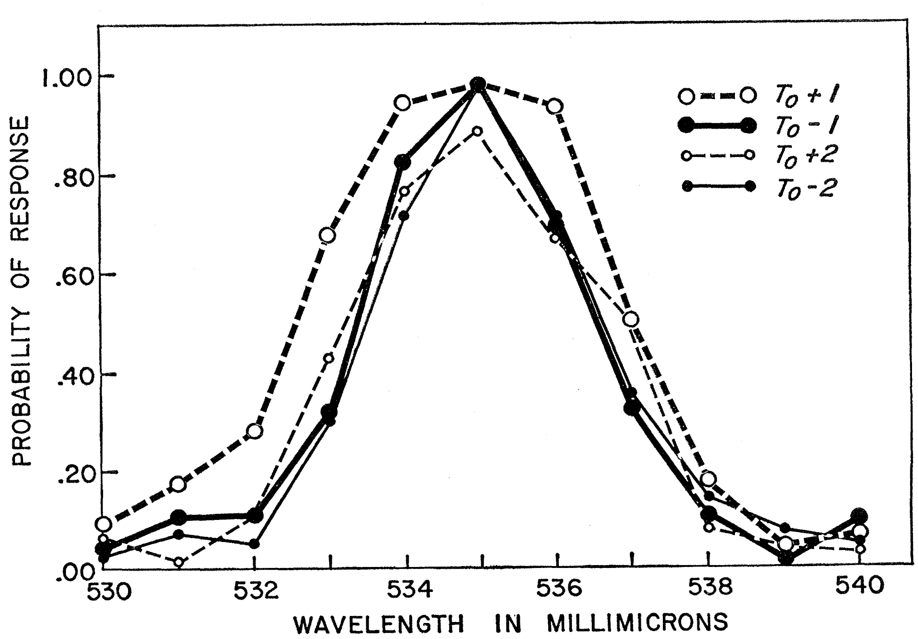

Fig. 2. Same as Fig. 1, but for second pigeon that was occasionaly rewarded for pecking in response to 535 mμ.

Note

1. Supported by grants MH 06661 and MH 08351 from NIH.

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