DNP (determined as DNA) of the original homogenate remained in the supernatant, whereas over 50 percent of the brain or liver DNP remained in the supernatant. If supernatants from the three tissues containing approximately equal concentrations of DNA (0.02 to 0.04 μmole of DNA-phosphorus per milliliter) were then made 0.15*M* in NaCl, let stand for 30 minutes, and then centrifuged for 30 minutes at 1500*g* (av.), over 95 percent of the erythrocyte DNP was precipitated, but less than 50 percent of the brain and liver DNP was precipitated. Erythrocyte DNP thus behaves like calf thymus DNP since it is highly insoluble in isotonic salt solutions.

Similar solutions of brain and liver DNP's, on the other hand, are not completely precipitated by isotonic salt, which is what one might expect of a set of DNA molecules that are less completely complexed with histones. It is conceivable that protease or deoxyribonuclease activity in the brain and liver homogenates prevented the DNP in these two tissues from sedimenting as easily in isotonic salt; however, an experiment in which the initial brain, liver, and erythrocyte homogenates were allowed to stand for 2 hours before their first centrifugation yielded essentially the same results. It must be emphasized that the above experiments were performed on tissue homogenates and thus alterations in the precipitability of DNP caused by other tissue proteins could not be completely controlled, but the highly dilute homogenates used should minimize these possibilities.

If we assume that the protein measured in the first set of experiments is actually part of the native DNP complex, then the results of both types of experiments would indicate that there may be different amounts of protein associated with the DNA of different tissues. If again we assume that the histone associated with DNA functions as an inhibitor of gene activity (*1*), then our results may be interpreted to suggest that the DNA's of brain and liver direct the synthesis of a greater variety of proteins than does the DNA of the erythrocyte; however, these interpretations are largely speculative, for it must be kept in mind that substances other than histone may play a role in the regulation of gene activity (*11*).

Although attempts were made to minimize and control for possible protease and DNase activity, it cannot be conclusively proved that they are not factors in our results. Further validation might be obtained by isolation and characterization of the native, undegraded DNP complex from brain, liver, and erythrocyte, although here, too, ultimate proof that the isolated material is truly native and undegraded will be difficult. There is a need for improved methods for isolating undegraded DNP's from a wide variety of tissues, in order to study this complex both structurally and functionally. Our results suggest that methods developed for one tissue are not necessarily directly applicable to another if one wishes to isolate a representative portion of the chromosomes from a given tissue (*12*).

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Errorless Discrimination Learning in the Pigeon: Effects of Chlorpromazine and Imipramine

Abstract. *Chlorpromazine or imipramine disrupts a pigeon's performance on a discrimination between a vertical and horizontal line only if the discrimination was learned with errors. Errorless learning is obtained if training starts with an easy-to-learn discrimination of color and shifts progressively to the more difficult horizontal-vertical discrimination.*

Recent experiments (*1*) have shown that a pigeon is able to acquire a discrimination of color and the orientation of a line without any "errors." An "error" is the failure to respond to the stimulus correlated with reinforcement (S+) or a response to the stimulus correlated with nonreinforcement (S−). Errorless learning is accomplished by starting discrimination training immediately after the response to S+ has been conditioned, and by progressively reducing the difference between S+ and S− from an initially large value to the relatively smaller final value.

When a discrimination is learned without errors, certain characteristics of performance, normally observed in discrimination performance after learning with errors, are lacking (*1*). These are (i) an increase in the rate (or decrease in the latency) of the response to S+, (ii) sporadic bursts of responses to S−, separated by long intervals of no responses to S−, and (iii) "emotional" responses to S−. The present study investigates another frequently observed characteristic of discrimination performance, the disruption of performance that follows the administration of certain drugs (*2*). Specifically, the effects of chlorpromazine and imipramine were studied after discrimination learning by the pigeon with, and without, errors. These drugs disrupt discrimination performance in the pigeon (*3*).

Discrimination training was carried out in a standard operant conditioning apparatus (*1*). The discriminative stimuli were projected on the response key during discrete, automatically programmed trials. Each trial was terminated by a single response or by the failure to respond within 5 seconds of the onset of the trial. A response that occurred during an S+ trial was immediately reinforced. Between trials, the "house light" remained on but the key was dark for intervals (mean length 30 seconds). S+ and S− trials alternated in random succession, unless an error was made, in which case the trial was repeated.

The subjects were four White Carneau male pigeons with no prior experimental history. Two pigeons (Nos.

75 and 100) were trained to discriminate between a vertical S+ and a horizontal S− line without errors. The details of the training procedure, which are described elsewhere (*1*), may be summarized as follows. Initially a red S+-green S− discrimination, which is easier to learn than the vertical-horizontal discrimination, was used to train the pigeons. At the start of discrimination training, S+ was a red key which was presented for 5 seconds. S− was a green key presented for 1 second. As training progressed the duration and intensity of S− was progressively increased until it equaled the duration and intensity of S+. In this manner the pigeons were trained to discriminate between red and green without any errors. After ten sessions of red-green training the discriminative stimuli were modified so that, on S+ trials, a white-vertical line was superimposed on the red key, and on S− trials, a white-horizontal line was superimposed on the green key. These compound stimuli presented during sessions 11 to 14 and during the first five trials of session 15. During trials 5 to 30 of the 15th session, the red and the green backgrounds of the compound stimuli were progressively faded out until only the vertical and the horizontal lines appeared as the discriminative stimuli. In this way, the pigeons were trained to discriminate between vertical and horizontal lines without any errors. Birds Nos. 75 and 100 each received 15 sessions of vertical-horizontal training, for a total of 30 discrimination sessions. During these sessions neither subject made an error.

The other two pigeons (Nos. 334 and 217) were trained to discriminate between the vertical and the horizontal lines without any progressive training. The vertical and the horizontal lines were the only stimuli to appear throughout their training. They made 860 and 1372 responses to S−, respectively, in 30 discrimination sessions. For both birds the probability of a response to S+ after the first conditioning session was always 1.0.

After 30 discrimination sessions had been completed for each of the four birds, each was given a series of discrimination trials after administration of a drug. Either chlorpromazine, imipramine, or physiological saline was injected intramuscularly every third day. On the two days between the administration of the drugs each bird was given further vertical-horizontal training. Four dose levels of each drug were used: 1, 3, 10, and 17 mg. The drug and the dosage to be used during each session were selected at random with the provision that a given dosage of each drug was to be used only twice. Each session began 30 minutes after the administration of the drug.

Table 1. Number of responses in pigeons to the S− stimulus during horizontal (S+)-vertical (S−) discrimination after being given injections of chlorpromazine or imipramine.

Dose (mg)	Responses (No.)			
	Bird No. 75	Bird No. 100	Bird No. 334	Bird No. 217
	Chlorpromazine			
1	0	0	5	76
	0	0	18	86
3	0	0	409	149
	0	0	421	235
10	0	0	496	272
	0	0	521	315
17	0	0	1325	862
	0	0	1514	1655
	Imipramine			
1	0	0	137	324
	0	0	161	207
3	0	0	544	522
	0	0	415	254
10	0	0	987	904
	0	0	2084	1186
17	0	0	3655	2651
	0	0	1872	2764

Table 1 shows the number of responses to S− emitted by each bird with repetition of a given dose or with increase in dose level of either chlorpromazine or imipramine. The duplicate values for dosage which appear consecutively in Table 1 represent responses at the first and second session, respectively, at that dosage. Table 1 shows very clearly that neither chlorpromazine nor imipramine had any effect on the performance of the two birds (Nos. 75 and 100) that had learned the vertical-horizontal discrimination without errors. The results also show that the performance of the other two birds was greatly impaired by both drugs at all dose levels. Neither of these two birds (Nos. 334 and 217) made more than eight responses to S− in ten sessions prior to, or on the days between the sessions in which the drug was administered. Injection of physiological saline had no effect on the performance of any of the birds.

Neither drug had any effect on the frequency of responses to S+. For all four birds the probability of responding to S+ remained at 1.0 during each session after drug administration. However, the latency of the response to S+ was, in each instance, lengthened as the dosages of the two drugs were increased. No systematic relation was observed between the effect of either drug on the latency of responding to S+ and the manner in which the vertical-horizontal discrimination was acquired.

The use of the correction procedure, repeating each trial during which an error occurred, makes it difficult to derive a dose-response curve from the data in Table 1. The correlation suggested by these data, between the dosage of a drug and its effect, may be attributed to an interaction between the length of a session and the duration of the effect of different dosages of a drug. Thus, it is possible that each dose has a similar effect on discrimination performance and that the larger effect of the larger dosages was the result of longer sessions stemming from the correction procedure. This possible artifact is currently being studied without employing the correction procedure.

The lack of any effect of both drugs on discrimination performance after learning without errors, argues strongly against explaining the disruption of performance, after learning with errors, in terms of a sensory deficit. An alternative explanation may stem from the aversive properties of extinction (*4*) that may be temporarily reduced by chlorpromazine or imipramine. When an extinction curve is obtained during the training of a discrimination, it is possible that S− acquires aversive properties. This is, presumably, not the case when a discrimination is learned without errors. The hypothesis that emerges from these assumptions is that chlorpromazine or imipramine, in the case of a discrimination learned with errors, reduces the aversiveness of S− and thus facilitated the pigeon's S− responses (*5*).

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