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EFFECTS OF DRUGS ON VISUALLY CONTROLLED BEHAVIOR IN PIGEONS

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INTRODUCTION

In this report I shall describe three behavioral techniques that appear to be useful for the study of drugs. Although I shall present illustrative data, my major aim is to call the methods to your attention. This research is only a small part of a substantial body of work along similar lines, yet I believe that this sort of methodology has a potential value that warrants still more widespread use.

Several of the laboratories involved in this work have found that pigeons are useful subjects for pharmacological research. DEWS[5] recently outlined some of the reasons for this choice of subjects. Among them are the pigeon's long life span, ease of care, and freedom from disease. More important are the years of study that have been devoted to behavioral analysis using the pigeon's conditioned pecking response[7]. This work supplies a rich background of behavioral data and research techniques on which the behavioral pharmacologist may draw. Of specific importance to the present experiments is the pigeon's excellent vision. This bird is easily conditioned to make discriminations among patterns and colors that would be difficult or impossible for the rat or most other small mammals. This fact makes the pigeon convenient to use in studies where the subject must respond to a variety of stimuli. It also opens the way for coordinated physiological research, for the physiology of the visual system is comparatively well understood.

How behavioral and physiological results may supplement each other may perhaps be seen in the case of the first experiment that I shall review. This research concerns the effect of LSD upon the absolute visual threshold of the pigeon.

EFFECT OF LSD ON THE VISUAL THRESHOLD OF THE PIGEON

The visual effects of LSD have aroused much interest. Included among these effects seems to be a decreased sensitivity to light. EVARTS[6] reported that heavy doses of LSD produce apparent blindness in monkeys and cats. He also found that LSD markedly reduced the postsynaptic response in the lateral geniculate nucleus to stimulus of the optic nerve of the cat. CARLSON[4] has observed that LSD raises the visual threshold slightly in man.

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Method

I have studied this problem in the pigeon with the aid of a method recently described elsewhere[1]. As in the other experiments I shall review, this method depends almost entirely on automatic apparatus. The experimenter administers a drug and places the bird in an enclosed chamber. Then electrical controls composed of relays, timers, and counters carry out the experiment and record the results. The pigeon's pecks on response keys produce electrical pulses that are recorded on charts or counters. An automatic magazine presents periodic food rewards to the pigeon. These rewards maintain the pigeon's responding during prolonged experimental sessions.

The present experiment is designed to find the minimum brightness at which the pigeon can see a luminous stimulus patch. Fig. 1 shows the arrangements that accomplish this. The hungry pigeon stands in a light-tight chamber and views a stimulus patch. The food magazine is moved within reach when the bird makes appropriate movements. In this way the bird is trained to peck on the two response keys, A and B. Once it has learned to respond to the two keys, the pigeon must be trained to peck only key A when it can see the stimulus, and to peck only key B when the stimulus is dark. It would take too long to tell in detail how this training proceeds. It must suffice to say that the pigeon learns this task in a relatively short time, and that the behavior may then be maintained indefinitely by appropriately rewarding the pigeon with a few grains of food 2 or 3 times a minute during each experimental session.

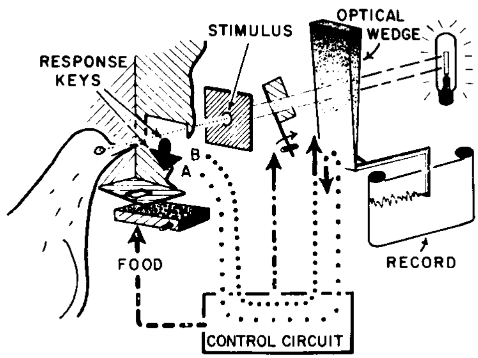

Fig. 1. Schematic diagram of absolute threshold apparatus.

Once the bird had learned to peck key A only when the stimulus is illuminated, and key B only when the stimulus appears dark, the automatic apparatus is adjusted in such a way that pecks on key A move the optical wedge down, decreasing the stimulus brightness, while pecks on key B move it up, increasing the stimulus brightness. These brightness changes are recorded on a moving chart as shown in Fig. 1. Threshold measurements are obtained as follows. The bird pecks key A until the stimulus becomes so dim that it falls below the bird's absolute threshold. But then, since the patch appears dark, the pigeon pecks key B. Pecking key B increases the brightness of the stimulus, and in a short time it again becomes visible to the bird. When this happens, the bird switches its pecking back to key A, causing the stimulus to dim and to disappear as before. This process continues indefinitely, the bird alternately pecks keys A and B, and the stimulus fluctuates up and down across the bird's absolute threshold. I might add at this point that the pigeon works in complete darkness; the only light comes from the stimulus itself.

Results

When the pigeon is dark-adapted and placed in the experimental apparatus, its pecks cause the recorder to draw a wavy line. When no drug is given, this line maintains a stable level for hours, indicating that the visual threshold does not change substantially during this time. However, if, after letting the bird work for half an hour, a small dose of LSD is administered, a striking change is produced. A sample of such an effect is shown in Fig. 2. Each curve shown is made up of three original records,

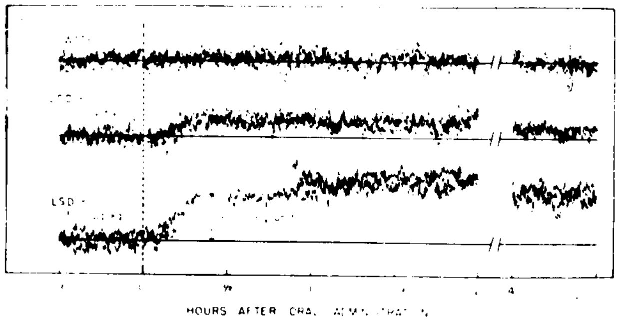

Fig. 2. Effect of orally administered LSD on one pigeon's absolute threshold. Vertical shifts in the curves represent changes in the brightness of a "just visible" stimulus patch. Each curve consists of three superimposed individual sessions.

each from a single session. At the top of the record water control sessions appear. Next are sessions in which 100 μg kg of LSD in water solution was administered orally to the bird. Finally the effect of 300 μg kg is shown. The threshold was traced for two hours after the doses were administered. Then the pigeon rested for approximately two hours and a final test was given. Some tests have also been run about one day after LSD administration, but these have never revealed any effect of the drug.

It is clear that in this bird the effect of LSD on the visual threshold is swift and striking. With the 300 μg kg dose the bird's threshold went up more than ten-fold. Increases up to 60-fold have been recorded. The effect is almost at its peak after half an hour in this pigeon, but with other birds reaction to oral dosage has been more delayed and not as pronounced. Intraperitoneal injection has always produced quick and striking effects.

It might be argued that the threshold changes we seem to see here are only apparent: that is, the pigeon's visual sensitivity is not changed, but, rather that LSD is causing the bird to peck the keys incorrectly. In reply, I might point out that such incorrect responding would be expected to increase the variability of the records, rather than produce the stable shift in the level that we see here. However, the next experiment that I shall describe supplies a better argument against the view that these results are due to "confusion" on the part of the pigeon. It shows that under

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certain conditions, the pigeon performs with greater accuracy under the influence of LSD than without the drug.

EFFECTS OF DRUGS ON CONDITIONAL DISCRIMINATION ON THE PIGEON

In the experiment I have just described, the stimulus light might be said to control the pigeon's responsing. This sort of stimulus control sometimes appears to be lacking in both psychotic and drug-influenced behavior. We often express this by saying that in these cases the behavior is "not appropriate to the situation". My second experiment is specifically concerned with the stimulus control of behavior and drug-induced changes in this control.

Numerous experiments have shown that a pigeon quickly masters a simple visual discrimination, such as pecking an illuminated key but not a dark key. Attempts have been made to disrupt such behavior with a variety of drugs, without much success. It appears that such a simple discrimination, when well learned, is very stable and difficult to alter with drugs. In order to provide a discrimination that is sensitive to drug effects, the present technique involves a more difficult task. It requires the pigeon to take two stimuli into account, instead of a single stimulus. For this reason it is called a "conditional" descrimination.

Method

The bird confronts two semicircular translucent response keys separated by a vertical partition, as shown in Fig. 3. The two keys and the edge of the partition are independently lighted. The pigeon's task is illustrated in the inset. If the center partition is

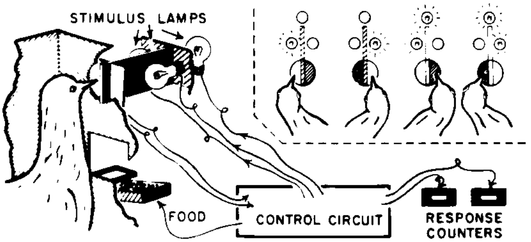

Fig. 3. Schematic diagram of conditional discrimination apparatus. Inset shows correct pecking behavior for each of the four stimulus combinations.

dark, pecks on the brighter of the two keys cause food to be presented to the bird. However, if the partition is lighted, the pigeon must peck the darker of the two keys to receive food. The stimulus array changes frequently in such a way that the left and right keys are correct equally often. Only a small proportion of pecks, even if they are correct, are rewarded with food. All pecks are recorded on counters that indicate whether they are "correct" or "incorrect".

Two measures of behavior are obtained in this situation: the total number of responses in a given time, and the percent of the responses that are correct. The first measure is related to more familiar "activity" scales. The second indicates the "accuracy" with which the bird pecks the keys, or, as we might say, it shows the extent to which the lights control the pecking of the keys.

After a dose of a drug is administered to a pigeon, and the bird is put into the experimental chamber, the apparatus periodically records the number of correct and the number of incorrect pecks. From this record a chart can be drawn, showing progressive changes in the behavior as the effect of the drug grows and then fades away.

Results

In my initial experiments with this technique, some interesting results have appeared. As an example, Fig. 4 compares the effects of oral doses of LSD (200 μg/kg) and

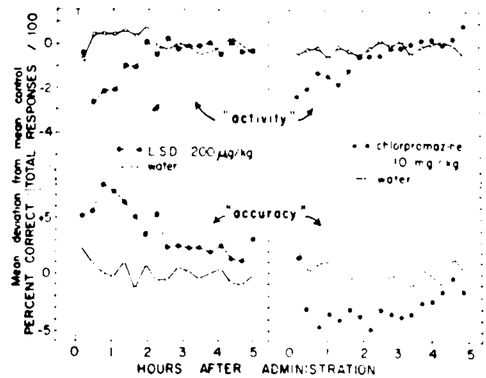

Fig. 4. Effects of drugs on conditional discrimination with time following oral administration. Each point represents responding during an 18-minute period.

chlorpromazine (10 mg/kg). Control data, recorded following doses of water, are included. Each curve represents the mean of five sessions, one from each of five pigeons. The "activity" measures appear at the top of the figure. These curves show the change in the total number of pecks during each successive 18 min period following the administration of the drug. In the case of both drugs, responding is slow at first and gradually becomes more rapid until the control level is approached. The effects of the drugs upon "accuracy" appear in the lower half of the figure. Here, the drugs have opposite effects. While chlorpromazine causes the birds to perform more poorly in the discrimination, LSD improves their performance above its control level. In each case this effect on accuracy appears to outlast the effect on response rate. The same patterns of change have also been obtained at higher dose levels.

The improvement of the pigeon's accuracy with LSD is interesting, in view of the finding that at about the same dose level the pigeon's visual threshold is elevated and also that LSD is commonly supposed to have disruptive psychological effects. It is perhaps significant that the effect of chlorpromazine upon accuracy is opposite to that of LSD. However, several other drugs have also reduced accuracy in the situation.

Pentobarbital, for example, has caused relatively much larger decrements in accuracy. Fig. 5 illustrates some effects of this drug and of ethyl alcohol. The figure also exemplifies individual differences that appear with the present method. Alcohol and pentobarbital were given orally to three birds. As before, variations in the response

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rate of the birds appear in the upper part of the figure, while percent correct is shown below. In this case the drugs produce similar response patterns. At these dose levels (pentobarbital—10 mg/kg, alcohol—1.6 g/kg) both drugs increase the "activity"

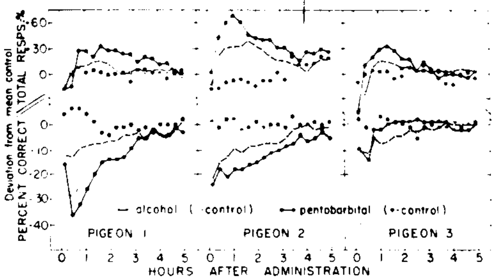

Fig. 5. Effects of alcohol (1.6 g/kg) and pentobarbital (10 mg/kg) with time following oral administration. Each curve represents the mean of 3 sessions. The unconnected circles and dots show data from water control sessions.

or response rate of the birds, while at the same time markedly decreasing the accuracy of their performance on the discrimination. These effects decrease in a regular fashion with time, and, at the end of 5 hours, they have almost disappeared. It is clear that the pattern of drug effects is to some extent unique for each bird. For example, Pigeon 1 showed much lower accuracy with pentobarbital than with alcohol, but in Pigeon 3 this difference is largely reversed. Pigeon 2 showed larger changes in response rate than did the other birds.

An example of the effect of different doses of a drug may be seen in Fig. 6. One

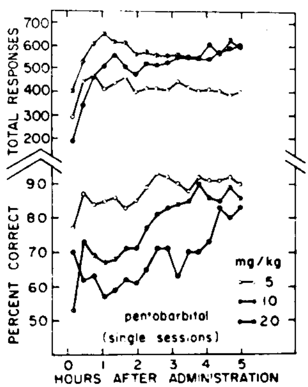

Fig. 6. Total response output and percent correct responses of one pigeon on 3 different experimental days. A different oral dose of pentobarbital was given each day.

pigeon received single sessions with each of three doses of pentobarbital-5, 10, and 20 mg/kg orally. Dose differences in the expected direction appear in the percent correct curves. The greatest response rate occurred after the medium (10 mg/kg) dose. This is not surprising in view of the fact that a very large dose would be expected to stop the bird's responding altogether.

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The effects of chlorpromazine recorded by this method were small, relative to those produced by comparable doses of pentobarbital. This relationship is reversed in the results of my third experiment, which involves a delayed discrimination or "immediate memory" aspect.

EFFECTS OF DRUGS ON DELAYED DISCRIMINATION IN THE PIGEON

At least two findings suggest that drugs may produce different effects on delayed discrimination than on simultaneous discrimination. First, these two types of discrimination have been shown to respond differentially to the locus of cortical lesions[8,9]. Second, a new test for human patients that contains elements of a delayed discrimination task has recently proven sensitive to chlorpromazine but not to several other drugs, including secobarbital[10].

Method

The delayed discrimination procedure that I have used with pigeons is illustrated in Fig. 7. The pigeon confronts a central stimulus bar located between two response

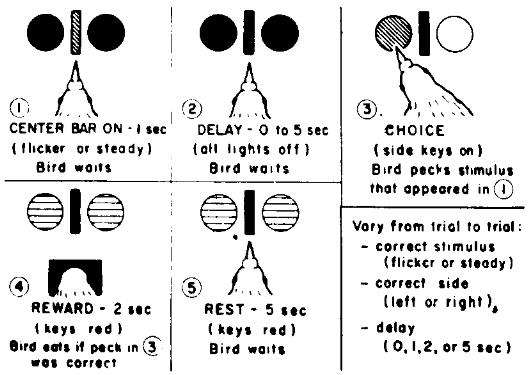

Fig. 7. Diagram of the course of events during one delayed discrimination trial

keys, a situation somewhat like that used in the experiment just described. However, the sequence of events is somewhat different in the present case. At the beginning of a trial, only the center bar is lighted. I shall call this bar the "sample" (1). The response keys are dark. The light on the center bar, or sample, is either flickering or steady. After 1 sec, this sample disappears and there is a delay period (2), during which neither the center bar nor the keys are lighted. After the delay, which may vary from 0 to 5 sec in length, the keys are illuminated (3). One key is flickering, the other is steady. The pigeon's task is to peck the key that matches the appearance of the sample seen before the delay. If the pigeon's choice is correct, it receives a grain or two of food (4), and a new stimulus sequence appears after a short "rest" interval (5). If the pigeon chooses the wrong key, it receives no food and the same stimulus sequence appears again after the rest interval.

Four hundred rewarded trials are presented in a typical daily session. In the course

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of these trials the delay interval (0 to 5 sec), the sample stimulus (flicker or steady) and the correct key (right or left) all vary randomly. The percentage of the bird's responses that were correct is calculated from response counters. Drugs or control doses of water are administered prior to each session.

Results

Some recent results appear in Fig. 8. The curves shown here relate the bird's accuracy of choice (percent correct) to the length of the delay between presentation of the sample stimulus and the pigeon's choice response. Each curve represents the mean of 18 individual daily sessions, 6 from each of 3 birds.

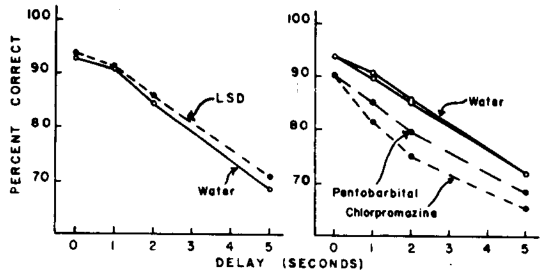

Fig. 8. Effects of drugs on percent correct response as a function of different delay intervals. The doses were intramuscular: LSD–50 μg/kg, pentobarbital and chlorpromazine – 5 mg/kg.

In the graph on the left the effect of 50 μg/kg LSD (intramuscular) appears in comparison with control sessions that were alternated with the experimental runs. The slight improvement in performance under the drug is in agreement with the results of the previous experiment, although the improvement appeared in only one bird, and the overall difference would not stand statistical scrutiny.

On the right are plotted results from equal doses of chlorpromazine and pentobarbital, together with their associated control curves. The similarity of the water control curves illustrates the stability of the behavior during the experiment. There are two features of the curves that have possible significance. (These features appear in the individual data of each pigeon.) First, chlorpromazine causes a larger decrement on this test than an equal dose of pentobarbital, reversing the effect found with the previous technique. Second, the larger decrement with chlorpromazine is evident only in the responses made after some delay, not in the simultaneous discrimination at 0 sec delay. This finding may indicate that the delay technique does indeed test somewhat different functions than does the simultaneous method.

DISCUSSION

In reviewing results such as those I have reported, it is tempting to draw analogies between the animals' behavior and human behavior—to predict, for example, that LSD will sharpen one's wits, or that chlorpromazine will impair one's immediate memory. I think it is a mistake to attach much importance to such reasoning, especially when the animal data have been gathered from species as remote from man as the pigeon. The more positive values of behavioral research with animals lie in other

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directions. To cite a familiar example, behavioral tests are commonly used in drug assays or screening. Behavioral data may also help us to classify drugs, by displaying similarities or differences in drug effects on various tests. Behavioral results may reveal general avenues of drug action, directing attention to changes in motivation, discriminative abilities, or emotional responsiveness, for example. These findings may suggest or supplement physiological results from the same species. Possibly the most far-reaching value of behavioral research with drugs is that it may lead us to a better understanding of basic laws governing the normal behavior of individuals of all species.

SUMMARY

In these pages I have described three techniques that are currently being employed in the study of drug effects in pigeons. I regret that I have been unable to review the large volume of related research that is proceeding in several laboratories using pigeon, rat, monkey and other animal subjects.

The techniques described seem to offer several advantages in the study of the behavioral effects of drugs. Two of the methods show the course of drug action through time. They all appear to be sensitive to drug dosages that cause few or no grossly observable behavioral effects. The effects obtained thus far are often visible in the data from single experimental sessions, and they appear to vary regularly with dose level. The techniques provide a variety of measures, giving a relatively high probability that different drugs will produce different patterns of effects.

It would be premature at best to attempt to generalize widely from the illustrative results that I have presented. Further data, covering a variety of dose levels, are clearly called for. A summary of the results follows. (1) LSD elevated the visual threshold of the pigeon substantially, at doses causing little or no motor disturbance and unimpaired discrimination. (2) LSD improved the pigeon's ability to perform a visual discrimination task, while chlorpromazine caused some decrement in the same task. Both drugs reduced the rate of the bird's pecking response. Pentobarbital and alcohol both seriously impaired accuracy on this task, while increasing the response rate. (3) Chlorpromazine and pentobarbital also produced decrements in the performance of a delayed discrimination. This delay technique appeared to be relatively sensitive to chlorpromazine. Data relating accuracy with length of delay indicate that chlorpromazine may affect delayed discrimination in a somewhat different manner than does pentobarbital.

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