Pharmacology Biochemistry & Behavior, Vol. 7, pp. 483–486.

BRIEF COMMUNICATION

Drug Discrimination and Generalization in Pigeons[1]

MARK R. LEBERER[2] AND STEPHEN C. FOWLER

Department of Psychology, University of Mississippi, University, MS 38677

(Received 28 February 1977)

LEBERER, M. R. AND S. C. FOWLER. *Drug discrimination and generalization in pigeons.* PHARMAC. BIOCHEM. BEHAV. 7(5) 483–486, 1977. – In a three-key operant conditioning situation six pigeons were trained to select the response key which was associated with each of three drug treatment conditons: d-amphetamine (2 mg/kg), pentobarbital (5 mg/kg), and saline. Thus, the drug state served as a discriminative stimulus for food reinforcement. After 20 sessions of discrimination training in each of the three conditions, more than 90% of the responses were correctly emitted in the presence of the appropriate drug or saline stimulus. Acquisition of the discrimination progressed at approximately equal rates for the three treatments. Subsequent to discrimination training, generalization gradients were obtained for several doses of the training drugs and for dose ranges of cocaine, morphine, and methocarbamol. The pigeons responded to morphine by choosing the key paired with pentobarbital during training; further, cocaine administration resulted in choice of the amphetamine key. However, methocarbamol, over the doses used, produced responding more characteristic of saline than of the other training drugs. The data suggest that a three-key operant discrimination procedure using pigeons provides a sensitive method for investigating the stimulus properties of relatively low doses of behaviorally relevant drugs.

Drug discrimination Pigeons Pentobarbital d–Amphetamine Cocaine Morphine Methocarbamol

THE PHYSIOLOGICAL state induced by a variety of psychoactive drugs has been shown to be an effective cue for animals in discrimination learning tasks [15]. Further, some authors have attempted to classify such drugs according to their discriminative properties [1, 12, 13]. There is some evidence that the observed discriminability of a drug may depend in part on the training dose [14], training task [8], route of administration [16], and species of test animals [3] used. Pentobarbital, for example, has been classified as more discriminable than amphetamine when T-maze shock escape procedures are used, while the reverse has been shown to be true when operant tasks have been selected [12,14]. In general, the available data suggest that procedures utilizing shock-escape as motivation tend to be less sensitive measures of discriminative control of differential responding than operant techniques using choice or conflict procedures [8]. For instance, Harris and Balster [5] used 1 mg/kg of amphetamine as a discriminative stimulus to obtain substantial control of lever choice and of performance in a multiple schedule of reinforcement while, in contrast, Overton [10,11] reported only moderate control with 5 mg/kg in a shock-escape T-maze situation. As a result of the comparative insensitivity of the shock-escape T-maze methods, recent studies have investigated, in several organisms, the scope of drug stimulus control by using a variety of free-operant procedures [2, 17, 18].

One objective of the research reported herein was to extend the prior findings in this area by describing the development of drug stimulus control among three different drugs using a three-key operant choice procedure instead of the two-alternative choice procedures used previously. If the parameters determining drug stimulus control are the same, by and large, as those determining exteroceptive stimulus control, then one would expect that a three-drug discrimination procedure would sharpen stimulus control [17].

A search of the literature reveals few studies describing the sensitivity of avian animals in either drug discrimination, drug-dissociation, or drug reinforcement paradigms. Bradford and MacDonald [3] found that chicks failed to display drug-dissociated learning in an imprinting situation. In contrast, Henriksson, Johansson and Jarbe [6], working with pigeons, found that 0.25 mg/kg, IM of Δ^9–THC could control differential responding in a two-key operant situation. Thus, because of the paucity of available data, the pigeon was selected as the experimental animal in order to assess further the possible usefulness of this representative avian species in drug discrimination research.

METHOD

Animals

The animals were six white Carneaux pigeons at least five years of age at the beginning of the experiment.

[1] This research was supported by HEW Grant MH–13570–03, Dr. W. F. Crowder, Principal Investigator.
[2] Reprints may be obtained from Mark R. Leberer, Department of Psychology, Fayetteville State University, Fayetteville, NC 28301.

Animals P102, P105 and P106 had previous experience in a matching-to-sample experiment. Animals P108, P206 and P207 were experimentally naive at the start of the experiment. Birds were maintained under constant illumination at 80% of their ad lib body weights.

Apparatus

The experimental chamber consisted of a standard LVE-Pigeon-Test-Chamber outfitted with a houselight and three transparent response keys. The left, center, and right keys were illuminated with green, white and red lights, respectively, using IEE rear-screen projectors. All recording and programming of events were controlled by electromechanical and solid state equipment located in an adjacent room.

Procedure

Initially, all animals were trained to peck a lighted key following the autoshaping technique of Brown and Jenkins [4], with one modification. Any one of the three keys was illuminated in a random sequence. This was done to condition approach responses to all three keys simultaneously and to ensure that approximately equal numbers of reinforcements were delivered in the presence of each of the three keys.

Following pretraining, all animals received the drug-discrimination procedure. On any particular day, either d-amphetamine (2.0 mg/kg, IM), sodium pentobarbital (5.0 mg/kg, IM) or 0.9% saline (injected IM) was administered 30 min prior to the initiation of the session. Under all conditions, the injection volume was 1.0 cc. During the 30 min period prior to the start of the session, the animals remained in the experimental chamber, with the houselight off and keys darkened. At the end of 30 min the houselight and keys were illuminated, and the subject was reinforced for pecking red, white, or green on amphetamine, saline, or barbiturate days, respectively. A particular key color was always associated with the same key position (left, center, or right) for each pigeon. Drugs were assigned to days according to a table of random permutations with the constraint that no two consecutive days could be run under the same drug condition. During each session, the number of responses on each key, both prior to and following the first reinforcement in each session, was recorded. The relative proportion of correct responses prior to obtaining the first reinforcement was taken to be an index of the degree of stimulus control exerted by a drug during any session.

Sessions lasted for 30 min or until the animal has earned 50 reinforcements, whichever occurred first. A reinforcement consisted of 2 sec access to Purina Pigeon Checkers. During the first five sessions, a fixed ratio 1: one response/reinforcement, was in effect for correct responses. From Sessions 6–20, reinforcement was available on the average of every 30 responses (VR30), with the constraint that the first ratio requirement was always 30 responses.

Animals were run under this drug-discrimination procedure for 20 sessions at each stimulus condition. This number of sessions resulted in a proportion of correct responses for each bird that was at least 0.90 with less than ±5% variation over the last five days.

Following stable performance on the drug discrimination task, Phase II generalization tests were initiated. During this phase, all subjects were administered a number of test drugs, each at various dosage levels. Again, all subjects were injected intramuscularly 30 min prior to the initiation of the session. Test sessions lasted for 30 min or until the animal had made 50 responses. While 30 responses were used as a measure of stimulus control during the training sessions, it was reasoned that a sample of 50 responses would be a more stringent test of stimulus control by drugs during the generalization tests. Indeed, if the stimulus control by the stimulus properties of the drug was weak, the probability of switching to another key after the first 30 responses would increase. Animals were never reinforced during test sessions. A record was kept of the responses emitted on each key during this period.

The various drugs and dosages used during generalization testing were: sodium pentobarbital: 2.5, 5.0 and 10..0 mg/kg, IM; d-amphetamine sulfate: 0.75, 1.5 and 3.0 mg/kg, IM; cocaine hydrochloride: 0.5, 1.0 and 2.0 mg/kg, IM; morphine sulfate: 2.5, 5.0 and 10.0 mg/kg, IM; methacarbamol: 2.0, 10.0 and 50.0 mg/kg, IM. Each of these doses was given only once in Phase II. Pentobarbital and d-amphetamine were used to validate the initial drug discrimination procedure since it was assumed that the intensity of the stimuli controlling responding would be a function of the dosage used. Cocaine, a local anesthetic judged by human users to be highly similar to d-amphetamine in its stimulant effects, would provide a test of the sensitivity of the procedure to generalization effects between drugs. In addition, cocaine was selected because it has not been extensively studied with drug discrimination procedures. Methocarbamol, thought to be a central muscle relaxant, was selected in an attempt to determine whether the muscle relaxant properties of sodium pentobarbital, in the doses used here, might be an important cue in the complex of stimulus changes which occur subsequent to its administration.

RESULTS

Figure 1 depicts the group mean performance for the six subjects during Phase I on the initial three-key drug discrimination. The values presented are the mean percent correct prior to the first reinforcement for each of the drug-stimulus conditions across 20 training sessions. By comparing the three [3] acquisition curves, it can be seen that all drug-stimulus conditions engendered approximately the same terminal degree of stimulus control, each curve asymptoting at over 90% correct. Further, all cues acquired control at about the same rate. Pentobarbital reached a terminal level of control in approximately 13 sessions, d-amphetamine in 15 sessions and saline in 15 sessions. These differences were found to be non-significant using a Friedman 2-way ANOVA by ranks ($X^2 = 3.99$, $N = 6$, $K = 3$).

The data for the Phase II generalization tests are expressed as the proportion of the total responses made on each of the three keys (Fig. 2). It can be seen that as the dose of pentobarbital or d-amphetamine was either increased or decreased, the mean proportion correct rose, or dropped accordingly. Further, such errors as were made at the lower doses were directed at the saline key not at the opposing drug key.

Further inspection of Fig. 2 shows that the birds reacted to the higher dose of morphine by responding more than 80% on the green (barbiturate) key. The lower doses of morphine were responded to as a saline cue. While the

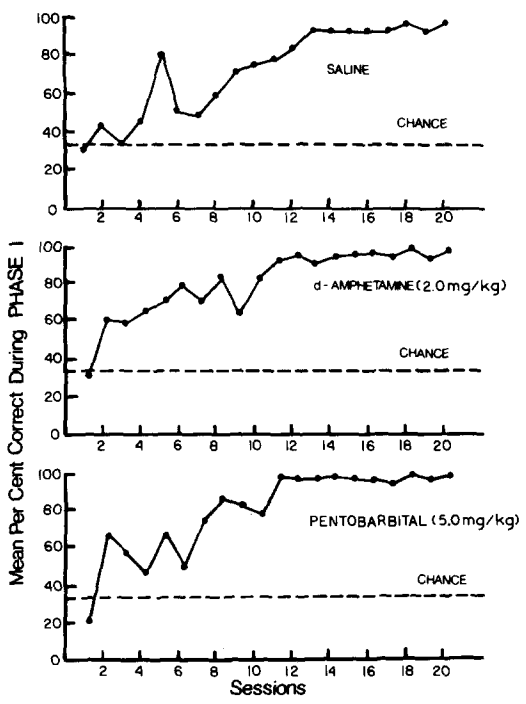

FIG. 1. Group mean discrimination acquisition curves for the indicated drug stimuli. The dependent variable is the percentage of correct responses made prior to the first reinforcement during a given session.

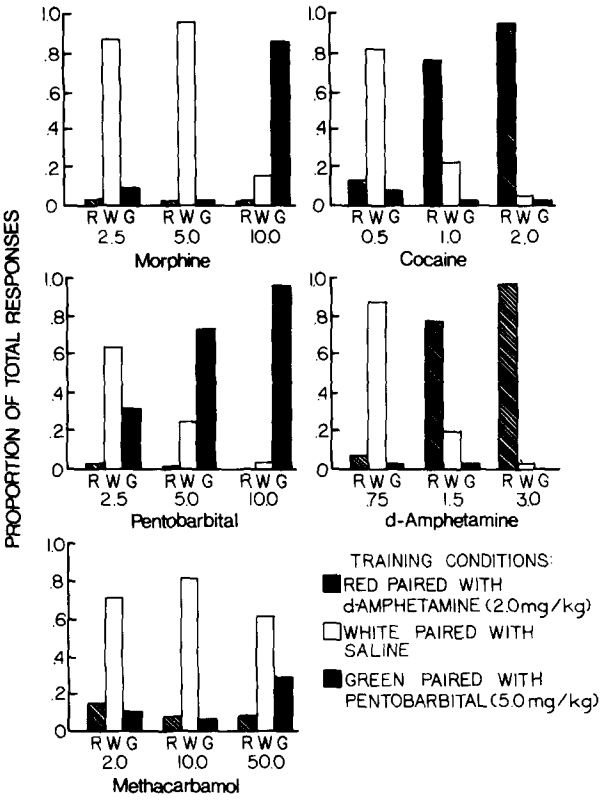

FIG. 2. Proportion of responses made during the Phase II generalization tests for the drugs and doses shown. The data are the mean performances for six animals.

highest dose of cocaine (2.0 mg/kg, IM) also induced strong amphetamine-like responding, there was still a small amount of responding to the saline key. Methocarbamol, a muscle relaxant drug, induced strong saline-like responding at all doses, although the greatest non-saline-like responding was on the key ordinarily associated with pentobarbital.

DISCUSSION

Figure 1 suggests that pigeons are able to discriminate three drug states in a free-operant situation. Previous drug discrimination studies using rats involving three choices in a discrete trial T-maze situation have yielded poor discrimination. For example, Overton's [9] rats attained only moderate (75%) performance levels with as many as 72 acquisition trails. Overton used phenobarbital (40 mg/kg), atropine (150 mg/kg) and saline as discriminative stimuli in a shock-escape procedure.

The acquisition data of the present study, as reflected by the proportion of responses made on the correct key prior to the first reinforcement, failed to reveal any significant differences in the rates with which saline, d-amphetamine or pentobarbital acquired control of responding. Previous T-maze shock studies have suggested pentobarbital to be a more potent discriminative stimulus than d-amphetamine [12,14]. Conversely, reported free-operant studies have suggested that d-amphetamine, in the doses used, is more potent. In the present study, where the acquisition of control by d-amphetamine, pentobarbital and saline can be observed concurrently in a within-groups design, no differences in discriminability among these conditions were seen.

During generalization tests, the animals' relative responding on the correct amphetamine or barbiturate keys varied appropriately with the dosage of the test drugs used. Substantial pentobarbital-like responding occurred for all doses of pentobarbital used, with the greatest proportion (96%) occurring at 10.0 mg/kg, IM. While the lowest dose of pentobarbital (2.5 mg/kg) induced some barbiturate-like responding (33%), most of the responding (62%) was on the saline key. Tests with d-amphetamine resulted in a similar profile: as the dosage of the training drug was increased, the relative proportion of responses on the amphetamine-like key also increased.

The pattern of key selection obtained with cocaine was highly similar to that observed for d-amphetamine at higher doses. At 2 mg/kg, IM cocaine, 95% of the responses were made on the d-amphetamine key. These data are consistent with the reports of human users of amphetamines and cocaine [7].

Overall, the present findings indicate that pigeons are capable of performing a three-alternative drug stimulus discrimination. Moreover, with the procedures used here it is possible to obtain both drug discrimination and drug generalization using doses considerably lower than those typically used in discrete trial T-maze work with rats. Finally, the finding that the pigeon generalizes between drugs which are usually classed as having similar psychotropic effects, suggests that these methods may prove relevant to understanding stimulus properties of drugs abused by human beings.

REFERENCES

1. Barry, H. Classification of drugs according to their discriminable effects in rats. *Fedn Proc.* **33:** 1814–1824, 1974.
2. Bliss, D. K., M. Sledjeski and A. Leiman. State dependent choice behavior in the rhesus monkey. *Neuropsychologia* **9:** 51–59, 1971.
3. Bradford, J. P. and G. E. MacDonald. The effects of sodium pentobarbital on the development of the approach responses in the domestic chick. Paper read at the Eastern Psychological Association Convention, New York, 1966.
4. Brown, P. L. and H. M. Jenkins. Autoshaping of the pigeons' keypeck. *J. exp. Analysis Behav.* **11:** 1–8, 1968.
5. Harris, R. T. and R. L. Balster. An analysis of the function of drugs in the stimulus control of operant behavior. In: *Stimulus Properties of Drugs,* edited by T. Thompson and R. Pickens. New York: Appleton-Century-Crofts, 1971, pp. 111–132.
6. Henriksson, B. G., J. O. Johansson and T. U. C. Jarbe. Δ^9-Tetrahydrocannabinol produced discrimination in pigeons. *Pharmac. Biochem. Behav.* **3:** 771–774, 1975.
7. Jaffe, J. H. Drug addiction and drug abuse. In: *The Pharmacological Basis of Therapeutics*, edited by L. S. Goodman and A. Gilman. New York: MacMillan, 1970, pp. 276–313.
8. Kubena, R. K. and H. Barry III. Two procedures for training differential responses in alcohol and nondrug conditions. *J. Pharmac. Sci.* **58:** 99–101, 1969.
9. Overton, D. A. Differential responding in a three-choice maze controlled by three drug states. *Psychopharmacologia* **11:** 376–378, 1967.
10. Overton, D. A. Dissociated learning in drug states (state dependent learning). In: *Psychopharmacology: A Review of Progress,* edited by D. H. Efron, J. O. Cole, J. Levine and R. Wittenborn. 1957–1967 (USPHS Pub., No. 1836). Washington, D.C.: U.S. Government Printing Office, 1968.
11. Overton, D. A. Control of T-maze choice by nicotinic, antinicotinic, antimuscarinic drugs. Proceedings of the 77th Annual Convention of the American Psychological Association, 869–870, 1969.
12. Overton, D. A. Discriminative control of behavior by drug states. In: *Stimulus Properties of Drugs*, edited by T. Thompson and R. Pickens. New York: Appleton-Century-Crofts, 1971, pp. 87–110.
13. Overton, D. A. State-dependent learning produced by alcohol and its relevance to alcoholism. In: *The Biology of Alcoholism: Physiology and Behavior,* edited by B. Kissen and H. Begleiter. New York: Plenum, 1972, pp. 193–217.
14. Overton, D. A. State dependent learning produced by addicting drugs. In: *Opiate Addiction: Origins and Treatment*, edited by S. Fisher and A. M. Freedman. Washington, D. C.: V. H. Winston, 1973, pp. 61–74.
15. Overton, D. A. Experimental methods for the study of state-dependent learning. *Fedn Proc.* **33:** 1800–1813, 1974.
16. Tomporowski, P. Cocaine as a discriminative stimulus in a T-maze task. Paper presented at the 21st Annual Meeting of the Southeastern Psychological Association, Atlanta, 1975.
17. Trost, J. G. and D. P. Ferraro. Discrimination and generalization of drug stimuli in monkeys. In: *Drug Addiction,* Vol. 3. *Neurobiology and Influences on Behavior,* edited by J. M. Sigh and H. Lal. Miami: Symposium Specialists, 1974, pp. 223–239.
18. Waters, W. H., D. W. Richards III and R. T. Harris. Discriminative control and generalization of the stimulus properties of d,l-amphetamine in the rat. In: *Drug Addiction: Experimental Pharmacology,* edited by J. M. Singh, L. H. Miller and H. Lal. Mount Kisco: Futura, 1972, pp. 87–98.