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ACKNOWLEDGMENTS AND ADDRESSES

Received July 22, 1968, from the *Medicinal Chemistry Laboratory, Pharmacy Research Institute, School of Pharmacy, University of Connecticut, Storrs, CT 06268*
Accepted for publication September 12, 1968.
Previous paper: A. Siciliano and K. Nieforth, *Arzneimittel-Forsch.*, **18**, 764(1968).
* Recipient of Lunsford-Richardson Undergraduate Research Award for stndy associated with this publication.
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Two Procedures for Training Differential Responses in Alcohol and Nondrug Conditions

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Abstract ☐ Two simple efficient procedures, automatically programmed in standard operant test chambers, are described for training rats to a high degree of response differentiation solely on the basis of the perceptual or sensory alterations caused by a drug. Rapid learning of differential approach and avoidance responses occurred with a Conflict procedure whereby hungry rats received food reward in one condition (1.2 g./kg. ethyl alcohol for seven animals, saline for seven animals) and shock in the other condition, after every fifth lever press. With a Choice procedure, a separate group of hungry rats learned to press preponderantly the food-rewarded lever during the initial, unreinforced portion of sessions in which they received food reward on an intermittent schedule for presses on one lever in the alcohol condition (left-hand lever for four animals, right-hand lever for four animals) and for presses on the other lever in the saline condition.

Keyphrases ☐ Differential responses—test procedures ☐ Alcohol, nondrug conditions—perceptual response differentiation ☐ Choice procedure—test method ☐ Conflict procedure—test method ☐ Equipment—differential response testing

The perceptual or sensory alterations caused by drugs enable animals to learn differential responses solely on the basis of whether they are in a drug or nondrug condition (1–10). Such learning may provide part of the explanation for the development of abnormal patterns of behavior under the influence of alcohol or other drugs (11). A technique for training animals to perform differential responses on the basis of their drug or nondrug condition may be used for investigating various problems of pharmacological interest. Problems which have been investigated include tests of similarities or dissimilarities in the perceptual or sensory effects of different compounds (2, 5), measurements of the threshold dose below which the animal cannot differentiate the drug from the nondrug condition (3, 5), and attempts to identify the central or peripheral alteration which is the basis for the differential responses in the drug and nondrug conditions (3, 5, 10).

The ideal training method would be a simple, efficient, automatic procedure which enables rapid learning of a high degree of response differentiation on the basis of a low drug dose compared to the nondrug condition. Most of the methods previously reported (1–6, 8, 10) have required the experimenter to place the animal into the choice situation at the beginning of each brief trial. The locomotor-choice response, measured in these procedures, is generally performed rapidly and hastily, to the detriment of the accuracy of the test. This is especially true of a shock-escape situation (2, 3, 5, 6, 10), in which rather high drug doses have generally been selected.

These disadvantages can be eliminated with the use of a lever-pressing response, in a standard operant test chamber. By means of an intermittent schedule of reinforcements, the test can be extended to require a substantial number of lever presses, thus providing a more deliberate choice by the animal and a wider range of quantitative variant on in the choice response. The prolonged test in an isolated chamber, with automatic programming and recording, provides an efficient procedure and also ensures that the experimenter cannot influence the animal's choice. However, the few operant methods previously reported have not provided simple efficient procedures for rapid learning of a high degree of differentiation of responses. Barry (7) associated food reward in the drug and nondrug conditions with differential environmental illumination, controlled by successive presses on the same lever. This procedure demonstrated that the rats learned a perceptual or sensory discrimination between the drug and nondrug conditions, thus refuting in this situation Overton's suggestion (3, 5) that separate, dissociated habits are learned in the drug and nondrug conditions. However, in this difficult task, the animals failed to achieve a highly consistent discriminative response, even after a large number of training sessions. Harris and Balster (9) reported on a complex procedure with only three rats, trained to choose different levers and at the same time different response rates in the drug and nondrug conditions.

The present paper reports on two simple efficient operant procedures, both designed to elicit rapid learning of a high degree of differentiation of responses on the basis of a moderate dose of ethyl alcohol compared to the nondrug condition. The first is a Conflict procedure, in which locomotor food-approach and shock-avoidance responses in a straight alley, used by Conger (1), are adapted to approach and avoidance of a lever-pressing response. The second is a Choice procedure, in which a locomotor choice between opposite arms of a T-maze, used by Barry *et al.* (4), is adapted to a choice between two levers.

METHODS

Subjects—The Conflict procedure was applied to 14 adult albino rats (Wistar descendants)[1] divided into eight males and six females. They were housed in individual cages in a room maintained at an average temperature of 22–23° (72–74° F.). Water was constantly available in the home cages. They were given 12 g. of Purina Lab Chow checkers daily, shortly after the testing time. For the Choice procedure, eight adult, male, albino rats were obtained from the same source and maintained under the same housing conditions and feeding schedule.

Apparatus—For the Conflict procedure, the operant test chambers[2] contained two levers on one wall with a food cup centered between them. The floor consisted of parallel steel bars 0.32 cm. (0.125 in.) in diameter, spaced 1.27 cm. (0.5 in.) apart. Electric shock (200 v.a.c.) was delivered through a 150,000-ohm resistor in a scrambled pattern to the floor bars, metal levers, and metal wall containing the levers and food cup. An unfrosted house light provided illumination throughout the session. Each chamber was enclosed in a cubicle. For the choice procedure, the chambers and cubicles[3] were similar but slightly larger, and in order to enhance the discriminability between the two levers, a frosted white light in the wall above the lever to the right of the food cup was continually on and provided the only illumination.

Procedures—The interval between sessions varied from 24 to 72 hr. Drug treatments and other experimental conditions were the same for the Conflict and Choice procedures except as otherwise noted.

The Conflict procedure began with preliminary training to press the lever to the right of the cup for food pellets (0.045 g.).[4] After the animals had learned to press the lever at a steady rate, usually following the second session, they were given 5-min. sessions of fixed-ratio reinforcement by delivery of a food pellet after every fifth lever press. Five minutes before the start of each session, including the preliminary training, seven animals were injected intraperitoneally with ethyl alcohol (1.2 g./kg. of a 10% v/v solution in 15 ml./kg. isotonic saline) and the other seven with the isotonic saline alone. Preparation of these solutions conformed to the recommendations by Barry and Wallgren (12). The alcohol dose was the same as in some of the prior studies (1, 4, 7) but only half the dose used by Overton (5). After two sessions of fixed-ratio reinforcement, the treatment prior to the next session was reversed (alcohol instead of saline or saline instead of alcohol), and every fifth lever press was followed by delivery of a painful electric shock throughout the time that the lever remained depressed, without delivery of food. In the subsequent sessions, both treatments were scheduled with equal frequency in a varied sequence.

In the Choice procedure, the eight animals were divided into four trained to press the lever to the right of the cup and four to press the lever to the left of the cup for food pellets. They were given four preliminary training sessions of reinforcement for each press, the first two preceded by saline injection and the next 2 by 1.2 g./kg. alcohol. In the alcohol sessions, food was obtained only by a press on the opposite lever from the one reinforced in the first two sessions. These were followed by 30-min. sessions of a 20-sec. fixed-interval schedule in which food reinforcement was obtained by the first press on the correct lever after 20 sec. had elapsed since the last prior reinforcement. The first two fixed-interval sessions were preceded by alcohol injection for four animals and by saline for the other four. Thereafter, two sessions under one condition were followed by two sessions under the other condition, so that each alcohol and saline session was preceded an equal number of times by a session under the same condition and under the other condition. Ten sessions with fixed-interval reinforcement, to establish a high rate of lever pressing, were followed by 20 sessions with a 1-min. variable-interval schedule, in which food was obtained by the first press on the correct lever after a variable interval, averaging 1 min., since the last prior reinforcement. The purpose of this final schedule was to train the animals to respond at a steady rate during prolonged absence of food pellets. No food was delivered in the first 1 min. of the 10 fixed-interval sessions and in the first 5 min. of the 20 variable-interval sessions. These initial unreinforced periods tested the performance of differential responses in the alcohol and saline conditions. The cup contained one food pellet at the start of each session, so that the animal's initial response was to approach the cup rather than one of the levers.

RESULTS

In the Conflict procedure, approach was defined as the completion of at least five lever presses during the 5-min. session, whereas avoidance was defined as failure to complete five presses. Figure 1 portrays performance during 20 sessions comprising 10 food and 10 shock sessions, beginning after the first shock session. The initial exposure to shock in the novel alcohol or saline condition resulted in approximately 50% approach response in the next few food and shock sessions. Learning of the differential responses is shown by gradual restoration of the approach response in the alcohol or saline condition associated with food while the approach response decreased in the opposite condition associated with shock. Statistical reliability of the differential responses is demonstrated with the use of the one-tailed binomial sign test (13); nine animals made the approach response whereas only one failed to approach in both of the last two food sessions ($p < 0.02$) and 12 animals failed to approach while none approached in both of the last two shock sessions ($p < 0.001$). Statistically reliable learning of the differential responses in the drug and nondrug conditions is demonstrated by an increase in the number of approaches in food sessions and avoidances in shock sessions from the first two to the last two sessions of each type for 11 animals, compared with a decrease in these responses for only one ($p < 0.001$). Performance was almost identical for the two groups of seven animals whose sessions of the same type (food and shock) were associated with the opposite alcohol and saline conditions. Likewise, no reliable difference was found between the males and females.

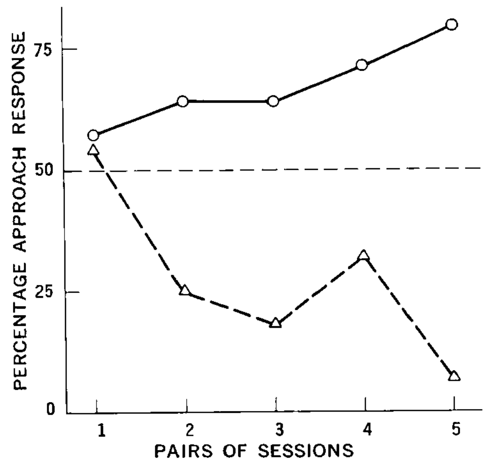

Figure 1—*Percentage incidence of approach response during food and shock sessions in the Conflict procedure, pooling together the groups of animals which received food in different conditions (alcohol and saline); both groups received shock in the other condition. Key:* O—O, *food;* Δ- - -Δ, *shock.*

[1] Hilltop Lab Animals Inc., Scottdale, Pa.
[2] Model 1316 and 1316c, Lehigh Valley Electronics, Inc., Fogelsville, Pa.
[3] Model 1417 and 1417c, Lehigh Valley Electronics, Inc.
[4] P. J. Noyes, Inc., Lancaster, N. H.

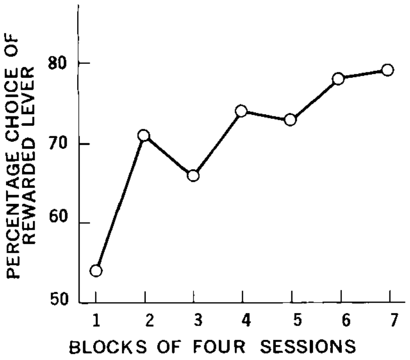

Figure 2—*Percentage preference for the correct, rewarded lever in the Choice procedure, pooling together in each block of four sessions, the two alcohol sessions in which one lever was rewarded and the two saline sessions in which the other lever was rewarded.*

In the Choice procedure, each animal's performance during the initial, unreinforced portion of each session was converted into a percentage preference score, representing the number of presses on the correct, reinforced lever divided by the number of presses on both levers. Figure 2 portrays these scores in the last 28 sessions, including the initial 1-min. period in the last eight sessions with fixed-interval reinforcement and the initial 5-min. period in all 20 sessions with variable-interval reinforcement. The preference score in all 28 sessions averaged together was above 50% for each of the eight animals ($p < 0.01$), indicating the performance of differential responses on the basis of alcohol or saline condition. Learning of the differential responses is shown by the fact that the average preference score increased from 54% in the first block of four sessions to 79% in the seventh block of sessions, with a higher preference score in the seventh than in the first block of sessions for each of the animals ($p < 0.01$). The average response rate in the seventh block of sessions was 16 presses/min. on the reinforced lever and seven on the unreinforced lever. Each block of four sessions included two alcohol and two saline sessions. There was no significant difference in performance between the alcohol and saline conditions, nor between the two groups of four animals which obtained food under the same condition by pressing opposite levers.

DISCUSSION

These two procedures have different advantages. The Conflict procedure enabled rapid learning of the differential responses in the drug and nondrug conditions, with the aid of a single-lever approach response and the association of drug and nondrug conditions with contrasting approach and avoidance responses. The brevity of the 5-min. sessions permitted efficient and economical use of the apparatus. However, the training and measurement of the differential approach and avoidance responses would be impaired if the drug had differential effects on these contrasting types of response. A behaviorally toxic drug might prevent the lever-pressing response, regardless of whether the drug condition was associated with food or shock. Conversely, a fear-reducing drug would tend to elicit the approach response, as reported for alcohol by Conger (1). A second disadvantage of the Conflict procedure was that the measure of performance did not provide quantitative variation in strength of the approach or avoidance response. The animals generally either responded rapidly or failed to press altogether, with few instances of long response latencies or making only some of the required five lever presses. In comparison with the Conflict procedure, the Choice procedure was more difficult and less efficient, due to the initial training to press both levers, the larger number of sessions, and the longer duration of each session. However, an important advantage of the Choice procedure was the use of equivalent responses, motivated by the same hunger drive, in the drug and nondrug conditions. The percentage of presses on the reinforced lever provided a quantitative measure of the strength of the choice response, independent of any drug effect on the rate of pressing the two levers combined.

Drug effects in most behavioral experiments are measured by differences from the control condition in probability or rate of responding. However, with both procedures reported in the present paper, these measures of performance showed no sizable differences between the alcohol and saline conditions. Conger (1) reported that a group of rats which received food in the alcohol condition and food plus shock in the saline condition learned differential approach and avoidance responses more rapidly than a group which received food in the saline condition and food plus shock in the alcohol condition. This differential learning gave evidence for an avoidance-reducing effect of alcohol, which has also been demonstrated in other conflict situations (14). Any such effect in the present Conflict procedure was apparently obscured by the rapid learning of the differential responses by both of the corresponding groups, perhaps because the avoidance condition consisted of shock without food reward. The present data also indicate that both procedures provide measures of drug effects at doses too low to cause readily detectable changes in performance. The alcohol dose (1.2 g./kg.) generally had slight effect on performance in studies reviewed by Barry and Buckley (14). Eickholt *et al.* (15), with the use of a higher alcohol dose (2.0 g./kg.), inferred rapid development of behavior tolerance from their finding that performance was impaired only in the first test after drug injection, with no statistically significant difference between drug and control animals in a series of subsequent tests. Such tolerance, which presumably developed in the present study after repeated alcohol injections, may account for the lack of alcohol effect on probability or rate of responding. The development of a high degree of response differentiation on the basis of drug condition, with both procedures described in the present paper, thus implies that these methods of training animals to respond on the basis of the perceptual or sensory alterations caused by drugs may provide sensitive measures of the effects of low doses.

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ACKNOWLEDGMENTS AND ADDRESSES

Received August 5, 1968, from the *Department of Pharmacology, University of Pittsburgh School of Pharmacy, Pittsburgh, PA 15213*

Accepted for publication October 1, 1968.

Presented in part at the 1967 and 1968 meetings of the American Psychological Association and at the 1968 meeting of the Federation of American Societies for Experimental Biology.

Abstracted in part from a thesis submitted by Robert K. Kubena to the University of Pittsburgh in partial fulfillment of Master of Science degree requirements.

Supported by a predoctoral traineeship sponsored under PHS training grant No. GM-1217 from the National Institute of General Medical Sciences (R.K.K.), and by a PHS Research Scientist Development Award No. K03-MH-05921 from the National Institute of Mental Health (H.B.).

Technical assistance was provided by Leonard Elias and by Linda K. Howdyshell.