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Conditioned Approach: An Analogue of Conditioned Avoidance; Effects of Chlorpromazine and Diazepam[1]

BERNARD MIGLER[2]

The Squibb Institute for Medical Research
Princeton NJ 08540

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MIGLER, B. *Conditioned approach: an analogue of conditioned avoidance; effects of chlorpromazine and diazepam.* PHARMAC. BIOCHEM. BEHAV. 3(6) 961–965, 1975. – An analogue of the conditioned avoidance test, the conditioned approach test, was designed in which the reinforcing event was eating food rather than avoiding or escaping shock. A response to the approach stimulus resulted in immediate delivery of food. Failure to respond to the approach stimulus for 15 sec resulted in the delivery of a food pellet. Administration of chlorpormazine at 2–4 mg/kg, PO to squirrel monkeys resulted in the failure of the monkeys to respond to many approach stimuli although they promptly responded to the freely delivered food pellet. Diazepam was without effect at doses up to 100 mg/kg, PO.

Conditioned approach Conditioned avoidance Chlorpromazine Squirrel monkey

THE report by Courvoisier *et al.* [3] that administration of chlorpromazine (CPZ) produced a greater deficit in shock avoidance behavior than in escape behavior in the conditioned avoidance (CAR) test has been confirmed by other workers [2].

The question to which the present study was addressed is whether CPZ or related drugs would produce a similar pattern of effects in an analogous test situation in which food reinforcement was used instead of shock avoidance or escape. An examination of the literature revealed a number of studies demonstrating deficits in behavior maintained by positive reinforcement [1, 5, 6] but none appear to have succeeded in designing a close analogue of the conditioned avoidance procedure. Specifically, a close analogue requires a test in which the subject is presented with a conditioned stimulus and reinforced if an appropriate response is made, or if no response is made after a fixed time interval, the unconditioned or reinforcing stimulus is presented and the subject may respond appropriately to it.

A test of this type using food reinforcement and the effects of CPZ and diazepam (DZP) on the resulting behavior are described in this report.

METHOD

Animals

Four adult squirrel monkeys (*Saimiri Scrureus*) were used.

Apparatus

Testing was conducted in a chamber measuring 33.5 cm on all sides housed within a larger sound resistant box. One wall of the test chamber contained a transparent plastic response disc (3.6 cm in dia.) installed 28.8 cm from the floor. A screw was installed in the disc and projected 2.4 cm into the chamber. Pushing the screw or pressing it down lightly caused the closure of a microswitch behind the disc. Colored lights were mounted behind the disc. Below and to the right of the response disc, a square hole 2.4 × 4.8 cm was cut in the wall 7.2 cm from the floor, and a food cup mounted behind the hole. A white light was installed in the cup and could illuminate its interior. A transparent plastic flap hinged at the top blocked access to the cup. To obtain a pellet of food in the cup, the monkey had to push the flap inward and grasp the pellet. Pushing the flap inward caused the closure of a microswitch. Food pellets (190 mg Noyes nutrient pellets) could be delivered from a pellet dispenser mounted on the roof of the outer chamber. Operation of the pellet feeder caused a loud noise due to the operation of a motor and a solenoid. A tone generator was mounted behind the wall containing the response key and food cup.

Procedure

Preliminary training consisted of a variable number of sessions in which the response disc was illuminated (with a tone present during the first second of the light) and remained on until a response to it was made, whereupon the light behind the response disc was extinguished, a pellet was delivered, and the food cup was illuminated. When the pellet was withdrawn a 1 min intertrial interval (ITI) was initiated. When responding to the tone plus light occurred

[1] The author wishes to express his appreciation to Mr. Richard Zinna for his expert technical assistance.
[2] Send reprint requests to Dr. Bernard Migler, Primate laboratory, The Squibb Institute, P.O. Box 4000, Princeton NJ 08540.

regularly, the final test procedure was begun. The final test procedure consisted of the illumination of the response disc with a yellow light for a maximum of 15 sec (with a tone present during the first second of the light) followed by the delivery of a free food pellet into the food cup, the illumination of the food cup, and the extinguishing of the light behind the response disc. When the flap in front of the food cup was pushed inward and released (the monkey presumably having taken the food pellet) the light in the food cup was extinguished and a 1 min ITI was initiated. At the end of the ITI the 1 sec tone was sounded and the response disc was simultaneously illuminated initiating a new trial. A response to the disc during its illumination resulted in the immediate delivery of a food pellet and illumination of the cup. The ITI began again with the operation of the flap. Thus, a response could be made to the illuminated disc resulting in the immediate delivery of a food pellet, or, if that response did not occur in 15 sec, the free food pellet could be taken. Sessions lasted 1 hr and were conducted 5 or 6 times per week. Following each session, the monkey was given ad lib food for 1 hr.

The above procedure will be referred to as the conditioned approach test. The intended relationship to the conditioned avoidance test is that in conditioned approach a response initiated by the discriminative stimulus (the approach stimulus) is equivalent to a response initiated by the discriminative stimulus, that is, the warning stimulus in conditioned avoidance, and, for those trials where no response occurs to the discriminative stimulus, a response initiated by the freely delivered food pellet and its accompanying stimuli in conditioned approach is similar to an escape response from the aversive stimulus in conditioned avoidance.

Drug administration. After stabilization of performance the effects of chlorpromazine hydrochloride (CPZ) and diazepam (DZP) were determined. The drugs were administered by oral gavage in a vehicle of 2 ml of water 30 min prior to a test session.

For 2 monkeys (Moishe and Sue) the effects of CPZ were determined by administering the drug for a single session after a number of sessions (usually 6) of baseline behavior had occurred. A range of doses were administered in mixed order with replications of doses of interest. For the third and fourth monkeys, JoAnne and Oscar, CPZ was administered in a series of daily increasing doses. The effect of DZP was examined in 3 monkeys, JoAnne, Moishe, and Oscar, by administering a series of daily increasing doses.

RESULTS

All 4 monkeys learned to respond promptly to the approach stimulus. Figure 1 presents frequency distributions of latencies of responses to the approach stimulus and to the free food pellet.

In the predrug session there were no instances in which the animal failed to respond to the approach stimulus. Following 1 mg/kg of CPZ, there were a few trials in which there was no response to the approach stimulus followed by a prompt response to the free food pellet. Following 2 mg/kg, the monkey failed to respond to the approach stimulus on many trials and in every case then took the free food pellet, usually rapidly as indicated by the heights of the bars just to the right of the dashed line.

Figures 2, 3 and 4 present frequency distributions of latencies of responses for JoAnne, Sue, and Moishe respec-

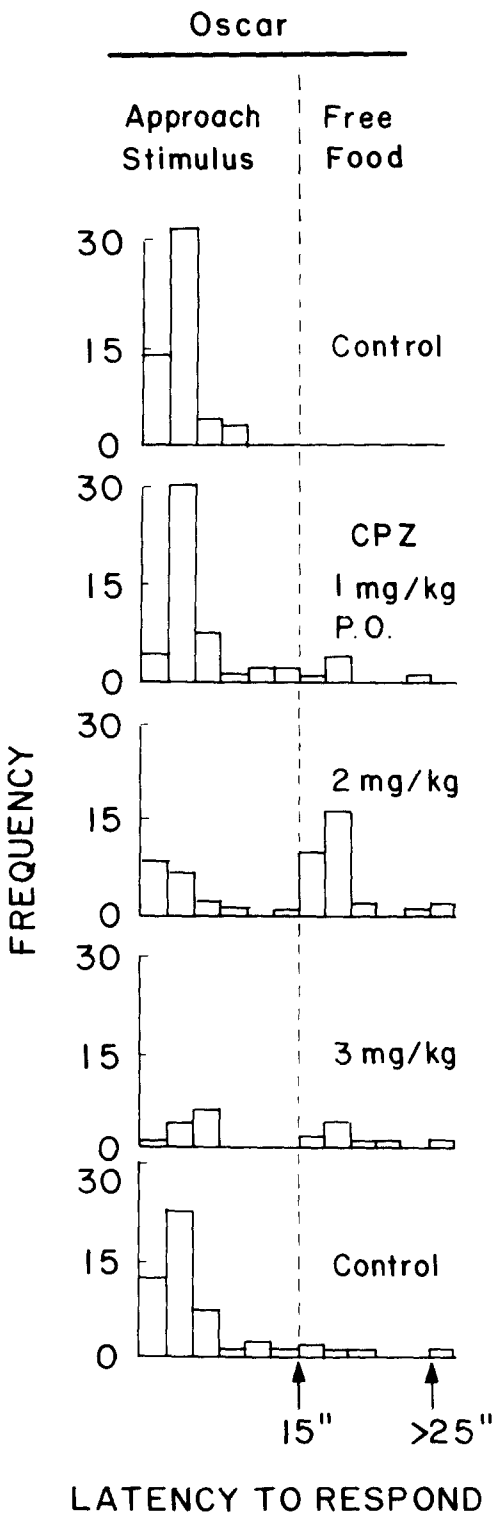

FIG. 1. Frequency distribution of latencies of responses from the onset of the approach stimulus to a key press (indicated on left side of dashed line) or to withdrawal of a free food pellet (right side of dashed line). Class intervals on the abcissa are two seconds wide except for the last interval during the approach stimulus which is five seconds wide and the last interval on the abcissa which records all latencies greater than 25 sec.

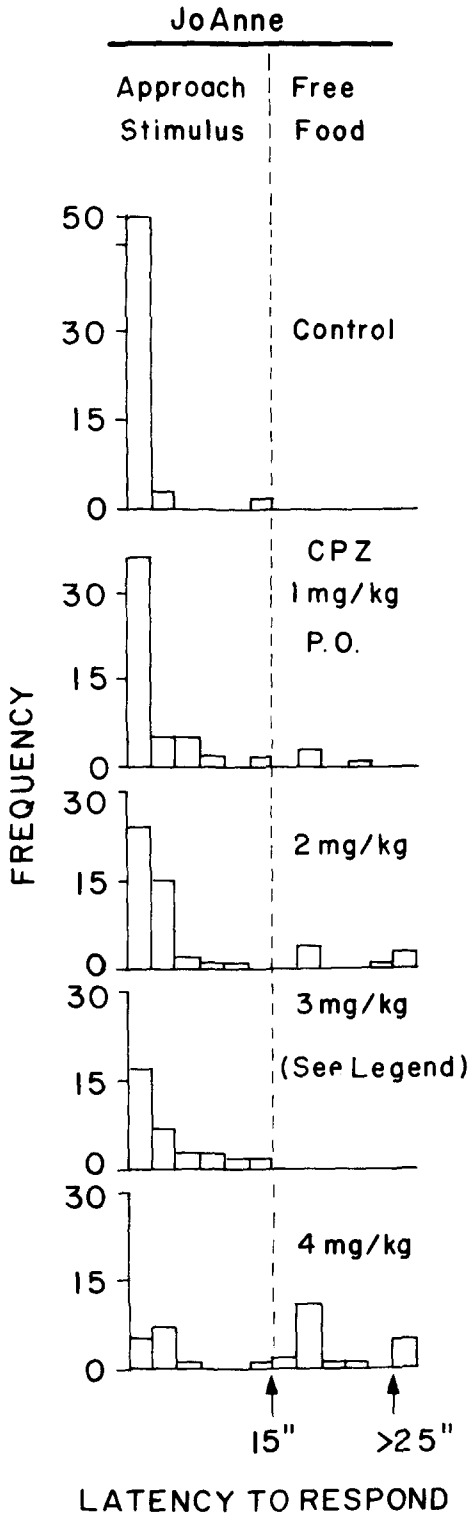

FIG. 2. Frequency distribution of latencies to respond to the approach stimulus or to the free food pellet. CPZ was administered in ascending daily doses. The latencies for responses to the free food pellets were accidentally not recorded for the 3 mg/kg session.

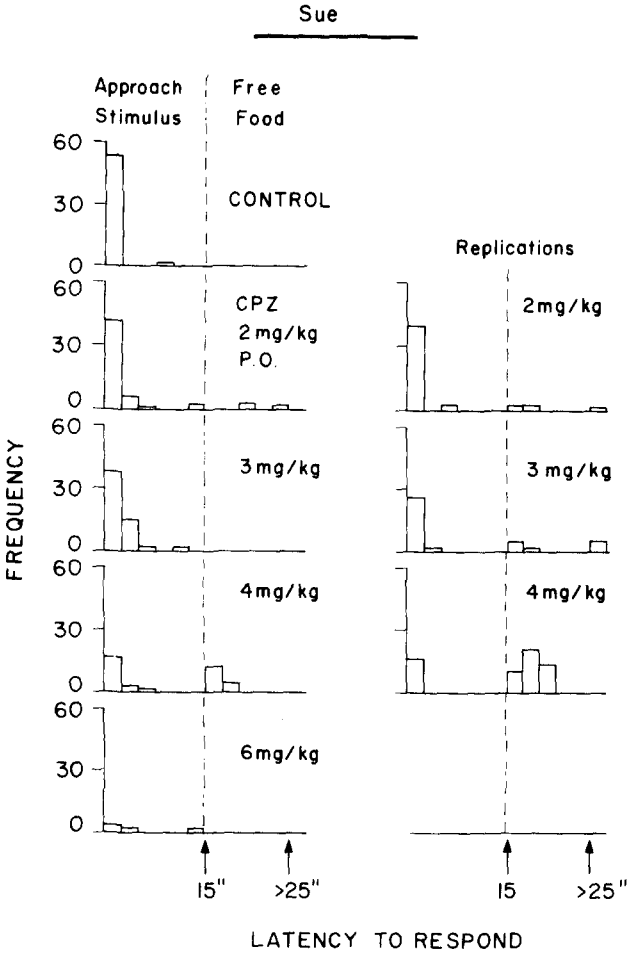

FIG. 3. Frequency distribution of latencies to respond to the approach stimulus or free food pellet. The various doses of CPZ were administered in a mixed order with control level of performance recovered prior to each drug session.

tively for 1 predrug control session and for sessions following administration of various doses of CPZ. For JoAnne (Fig. 4), the drug sessions were run in daily ascending doses. For Sue and Moishe, the doses were administered in a mixed order with baseline performance recovered prior to each drug session. Replications are shown in the right halves of Fig. 5.

For each monkey, CPZ at certain doses resulted in the failure of the monkey to respond to many of the approach stimuli followed by a short latency response to the free food pellet. At higher doses, they failed to respond even to the free food pellet.

The effect of DZP on conditioned approach behavior is shown in Fig. 5. DZP was administered in slowly or rapidly ascending daily doses to each monkey as indicated in the Figure. The animals continued to respond quickly to the approach stimulus even at doses up to 100 mg/kg, although the animals were ataxic in many of the sessions.

DISCUSSION

The results showed that in the conditioned approach procedure CPZ at certain doses markedly reduced the

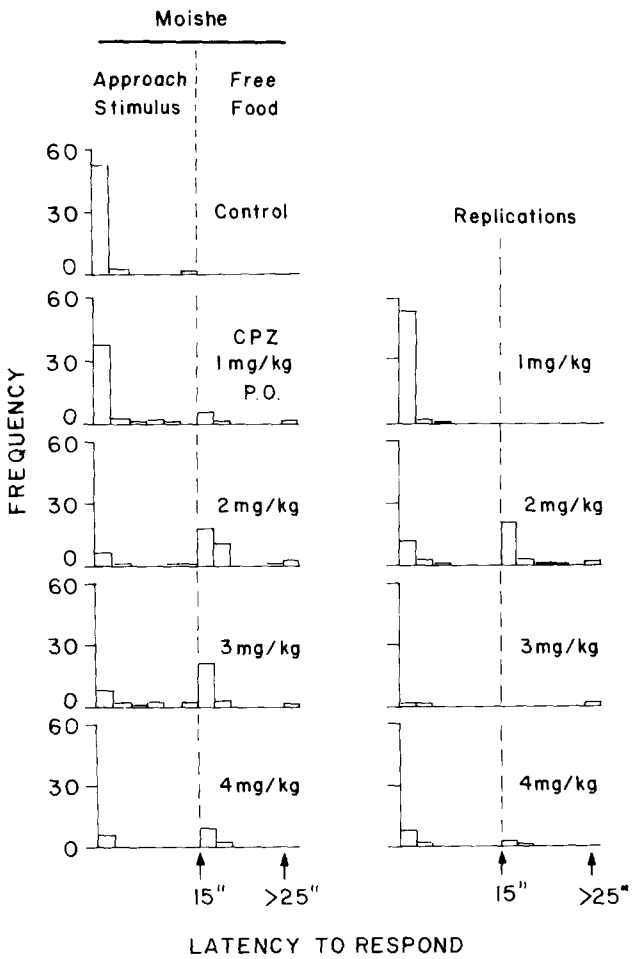

FIG. 4. Frequency distributions of latencies to respond to the approach stimulus or to the free food pellet. The various doses of CPZ were administered in a mixed order with control level of performance recovered prior to each drug session.

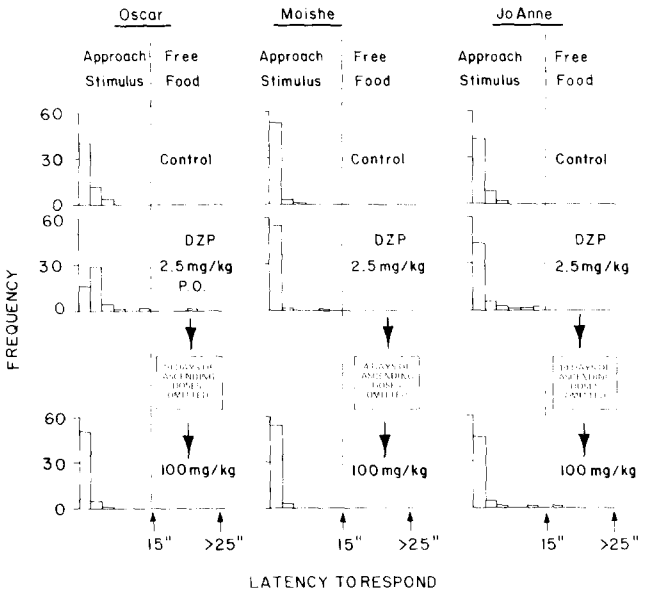

FIG. 5. Frequency distributions of latencies to respond to approach stimulus or free food pellet following oral administration of DZP ascending daily doses to 3 monkesy. For brevity, the data for 7, 7.5, 10, 15, 20, 25, 30, 35, 50, and 75 mg/kg doses are omitted for Oscar and JoAnne and for 10, 25, 50, and 75 mg/kg doses for Moishe. None of these doses had notable effects on the distribution of response latencies. Sue was accidentally doses with 10 mg/kg of tetrabenazine midway through her series of ascending daily doses of DZP and her data are, therefore, not presented. (Tetrabenazine produced a CPZ-like effect).

frequency of responses to the approach stimulus while preserving short latency responses to the free food pellet. DZP, even at 100 mg/kg, PO, did not produce this effect. On the basis of the formal similarity of the conditioned approach and conditioned avoidance procedures and the similar effects of CPZ in both tests the conditioned approach test may be regarded as a close analogue of the conditioned avoidance test. Furthermore, since CPZ produces similar effects in conditioned approach and conditioned avoidance it may be concluded that the nature of the effect of CPZ on CAR is not a specific antagonism of avoidance behavior, but is a more general behavioral effect. The nature of this effect remains to be elucidated.

Two possibilitites may be considered. First CPZ may reduce responsiveness to discriminative stimuli (i.e., the approach and warning stimuli) more than it reduces responsiveness to unconditioned or reinforcing stimuli (food and shock). Second, recalling that the delivery of food in the present procedure was accompanied by a sharp noise from the operation of the pellet feeder and solenoid, CPZ may act in these tests by reducing responsiveness to low intensity or weakly arousing stimuli (i.e., the approach and warning stimuli) more than it reduces responsiveness to strongly arousing stimuli (i.e., the loud sound of the pellet feeder and the shock).

Dews and Morse [4] suggested that the general behavioral deficit resulting from administration of CPZ was a reduction in responsiveness to stimuli, and more specifically that "the effects of CPZ would be seen first (in the sense of lowest dosage) on the response to the stimulus of least efficacy." However, no definition or measure of stimulus efficacy was suggested. The determination of stimulus efficacy at present would appear to be the relative susceptibility of different stimuli to drug effects. Without a definition or an independent measure of stimulus efficacy the term lacks explanatory or predictive usefulness. One possible measure of relative stimulus efficacy might be relative stimulus intensity. That is, the effects of CPZ would be seen first (in the sense of lowest dosage) on the response to less intense controlling (i.e., conditioned or unconditioned) stimuli.

A test of this hypothesis would be a study of the susceptibility to CPZ of different intensities of the warning stimulus in conditioned avoidance. Posluns [7] reported that avoidance behavior to loud versus low intensity auditory warning stimuli were equally affected by CPZ. However, he allowed only 5 sec for a response, and his loud stimulus was only 70 db, which is not very loud. A second test would involve a reversal of the intensities of the conditioned and unconditioned stimuli. While this is not possible for the conavoidance test it is possible for the conditioned approach test.

Another possible measure of relative stimulus efficacy is relative latencies of responses to different controlling

stimuli. That is, the effects of CPZ would be seen first (in the sense of lowest dosage) with stimuli that evoked longer latency responses than with stimuli that evoked shorter latency responses (reinforcement contingencies being identical). This possibility appears not to have been studied explicitly to date.

While the nature of the behavioral effect following CPZ administration is still not clear, it is anticipated that further testing of specific definitions of stimulus efficacy will further the analysis. In this, the conditioned approach procedure may be of use.

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