The Effect of Chlorpromazine on Behavior Maintained by an Escape Contingency and Fixed-Time Delivery of Shock

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THE EFFECT OF CHLORPROMAZINE ON BEHAVIOR MAINTAINED BY AN ESCAPE CONTINGENCY AND FIXED-TIME DELIVERY OF SHOCK

by

James P. Cleary

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Faculty of The Graduate College
in partial fulfillment of the
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Department of Psychology

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Kalamazoo, Michigan
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James P. Cleary
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INTRODUCTION

Chlorpromazine, a neuroleptic of the phenothiazine group, has been used to treat schizophrenia since 1952. Although its clinical efficacy and its impact on neurological research is generally recognized, its effect on behavior and its neurochemical mode of action have continued to be studied (Carlsson, 1978).

During early clinical tests on schizophrenics, phenothiazines were noted to have side effects that resembled the motor disorders characteristic of Parkinson's Disease. The correlation between the antipsychotic efficacy and the degree of extra-pyramidal side effects produced by these drugs provided a key insight to the mechanism of action of the phenothiazines (Deniker, 1970). In 1960, Hornykiewicz discovered that dopamine (DA) was depleted from the corpus striatum of patients with Parkinson's Disease. To test the hypothesis that DA depletion was responsible for the extra-pyramidal symptoms of the disease, he administered the dopamine precursor, L-dopa (3-4 dihydroxyphenylalanine), to Parkinsonian patients and noted a brief remission of their symptoms (Hornykiewicz, 1974). Since the phenothiazines were known not to lower brain dopamine levels in animals, this important discovery did not immediately explain the ability of the phenothiazines to produce extra-pyramidal effects. An important piece of the puzzle came when Carlsson and Lindquist (1963) discovered that the DA turnover rate was increased after chlorpromazine (CPZ) administration.
Carlsson suggested that CPZ blocked postsynaptic DA receptors, causing more DA to be synthesized and released; thus, keeping brain DA levels normal while increasing the DA turnover rate (Creese, Burt, & Snyder, 1978). This suggestion proved both correct and useful.

Perhaps the first direct evidence that neuroleptics might act as postsynaptic DA receptors was provided by Kababian, Petzold, and Greengard (1972). These investigators identified an adenylate cyclase in the homogenate of rat brains that was sensitive to DA stimulation. Dopamine caused accumulation of cyclic adenosine monophosphate in this homogenate. Subsequently, the neuroleptics were found to inhibit this DA sensitive adenylate cyclase (Miller, Horn, Iverson, & Pinder, 1974). The clinical potency of the individual phenothiazines correlated well with their ability to block the DA sensitivity of the adenylate cyclase. Thus, dopaminergic systems were strongly implicated as being directly involved in the neurochemical activity of the neuroleptics.

Further evidence in support of neuroleptic affinity for DA receptors was offered by several investigators (Creese, et al., 1978; Seeman & Lee, 1975). These former authors used labeled (3H) haloperidol and (3H) dopamine to compare many of the neuroleptics on the basis of their competition for DA receptor sites. If a particular drug prevented (3H) DA from binding with a membrane, it was assumed that the two were competing for the same receptor sites. The degree of competition appeared to correlate well with the phenothiazine drugs' clinical potency (Creese, et al., 1978).
Since anticholinergic drugs block the extrapyramidal effects of the neuroleptics in the striatum, it has been suggested that the neuroleptics' antipsychotic effect is in DA rich mesolimbic structures (Carlsson, 1978). This apparent anatomical separation of motor and antipsychotic effects is also supported by behavioral evidence.

Early behavioral experiments with nonhumans questioned the sedative theory of neuroleptic action. Cook and Weidley (1957) showed that CPZ reduced avoidance responding at doses that had no effect on escape responses. Although CPZ may induce catalepsy at high doses and generally reduces responding for positive reinforcers (e.g., Boren, 1961), its "selective" effect on avoidance argues against the notion that CPZ's primary action is as a motor depressant.

The selective action of CPZ reported by Cook and Weidley (1957) held special appeal for motivational theorists whose interpretations were based on clinical uses of CPZ (e.g., Miller, Murphy, & Mirskey, 1957). Motivationally, the aversive stimulation used in conditioned avoidance and escape procedures was thought to engender fear or anxiety in the organism. Chlorpromazine allegedly acted upon these underlying emotional components (Kelleher & Morse, 1964). A comparison of the effects of CPZ and other neuroleptics on behavior controlled by aversive consequences with the effects on behavior controlled by positive reinforcement could be used to test this hypothesis. However, although such comparisons indeed may contrast behaviors with and without "fear" components, their interpretation is rarely straightforward. For example, similar rates and patterns
of responding have rarely been produced under schedules of negative and positive reinforcement and, at minimum, this would be required for an unambiguous demonstration that drug effects differ as a function of the consequences maintaining behavior (e.g., Morse & Kelleher, 1977).

In general, CPZ has been found to reduce responding maintained by negative reinforcement in a variety of species, including man. Stone (1964), using rats, reported that responding under a continuous avoidance schedule was reduced and the number of shocks delivered was increased when rats were given doses of CPZ ranging from 2 mg/kg to 4 mg/kg. At 1 mg/kg, responding was little affected. Reduced avoidance responding after CPZ administration has been reported in monkeys (Hanson, Stone, & Witoslawski, 1970) and humans (Fischman, Smith & Schuster, 1976), and a selective decrease of avoidance responding compared to escape responding has consistently occurred. The selective effect of CPZ on avoidance at doses that do not affect escape has been attributed to decreased sensitivity (Irwin, 1958), fear reduction (Miller, et al., 1957), and motor depression (Posluns, 1962). The magnitude of the suppression produced by CPZ has been shown to decrease as a direct function of CS-US interval size (Low, Eliasson, & Kornetsky, 1966) and ease of acquisition of the avoidance response (Latz, Bain, & Kornetsky, 1969). Clark and Steele (1963) showed that response rates in animals that displayed post-shock bursts on Sidman (1953), avoidance was less affected by CPZ than rates in animals that did not show this response pattern. These authors suggested that post-shock bursts were behaviorally similar
to escape responses. Thus, CPZ's inability to block escape responses while suppressing avoidance was a function of its behavioral inactivity in regard to post-shock response bursts.

Depending on circumstances, CPZ can produce either rate decreases or rate increases under schedules of positive reinforcement. Cook and Kelleher (1962) reported that CPZ (1.0-2.0 mg/kg) decreased responding by pigeons under a variable-ratio 100 schedule of reinforcement, while increasing response rates on a key that signalled whether food was available under the variable-ratio schedule. Pigeons responding under a multiple fixed-ratio 30, fixed-interval 5 minutes food reinforcement schedule at doses of from 3.0 to 30.0 mg/kg, showed response decrements in fixed-interval response rates while responding slightly faster under the fixed-ratio component (McMillan, 1971). Such results have detracted from motivational interpretations of neuroleptic drug effects which seem to be of little value in explaining the actions of such drugs under schedules of positive reinforcement.

When positively reinforced behavior is periodically punished by electric shock, CPZ administration has had mixed effects on response rate. Dinsmoor and Lyon (1961) reported that CPZ (2 mg/kg) increased the relative rate of punished responding in rats. However, since the overall rate of responding was decreased by CPZ, the drug might best be thought of as maintaining the punished rate rather than increasing it. Looking at absolute rates in rats given CPZ (0.5-3.0 mg/kg), Geller, Kulak, and Seifter (1962) showed reduced rates of responding for food when responses were concurrently punished by
electric shock. Kelleher and Morse (1964) reported similar results. McMillan (1973b) clarified the factors controlling CPZ's effect on punished responding by showing that the effect on rate was both dose and rate dependent. Increases in punished rate were shown only at high doses and only when rate was severely suppressed in the baseline condition. Rate-dependent effects for CPZ (3.0–30.0 mg/kg) on both punished and unpunished responses in pigeons have also been convincingly demonstrated (McMillan, 1973a). In this study, low rates of both punished and unpunished responding were increased by CPZ while high rates were generally decreased.

Many of the studies discussed above examined the influence of neuroleptics on behaviors controlled by response-contingent removal or delivery of aversive stimuli. Hutchinson (1977) has demonstrated that complex patterns of responding may also be generated in situations that lack a contingency, as a direct effect of the aversive stimulus itself. When an aversive stimulus, such as electric shock, is repeatedly delivered in a regular temporal pattern, response sequences may become quite regular (Hutchinson, Renfrew & Young, 1971). The specific behaviors that occur may include sensory scanning, manual manipulative, and locomotor sequences (Hutchinson & Emley, 1972). Under schedules of fixed-time shock delivery, monkeys have been shown to produce patterns of biting, lever pressing, and chain pulling, similar to those characteristically educed by escaped-avoidance schedules (Hutchinson, et al., 1971). However, few comparisons of drug effects on similar patterns of behavior maintained by aversive stimuli delivered under response-dependent and response-independent schedules have been reported.
In an investigation of drug effects on biting attack and manual motor reaction, Emley and Hutchinson (1972) administered CPZ (0.06-1.0 mg/kg) to squirrel monkeys that were receiving response-independent shock every 4 minutes. These investigators found that CPZ significantly increased lever pressing, which regularly preceded shock but did not affect it, but decreased the biting that regularly followed shock. Since biting predominately occurred just after shock and lever pressing just before, the authors suggested that one possible action of CPZ is to shift response tendencies from post-shock aggression toward pre-shock anticipatory responding.

The present experiment was designed to investigate the effects of CPZ, in rats, on responses maintained by fixed-time presentation of shock, with and without an escape contingency. Important dependent variables to be compared in drug and nondrug sessions were escape latencies, number of post-shock response bursts, alterations in the temporal pattern of responding, and rates of responding. Previous studies have indicated these variables to be useful indicators of drug effects; they are also of theoretical significance (Hutchinson, 1977).
METHOD

Subjects

Six male Sprague-Dawley rats, obtained from the UpJohn Company, Kalamazoo, Michigan, were individually housed and given free access to food and water in the home cage. The subjects were approximately 150-days-old at the start of the study and were experimentally naive. A 12-hour light-dark cycle was maintained in the colony room throughout the experiment.

Apparatus

Three restraint tubes similar to that described by Azrin, Rubin, and Hutchinson (1968), but with several modifications, were used. They consisted of three separate parts: a baseplate, a restraint tube, and a removable cap to which was affixed the response manipulandum (see Figure 1).

The baseplate was constructed of 12mm clear plastic and was 20cm x 42cm. It served to mount the restraint tube firmly and to support the electrodes that delivered shock to the tail of the animal. When the subject was restrained within the tube, the tube snapped onto the baseplate such that the subject's tail was positioned beneath two aluminum shock electrodes (12cm x 1cm x 1cm) which were mounted on a stockade affixed to the baseplate. The electrodes were hinged so that they could swing down and lightly make contact with the subject's tail. At the point of contact with
the tail, part of the electrode was filed so that a concave surface fit over the rat's tail; thus, increasing the area of contact. When in contact with the tail, the electrodes were 2.5 cm apart. Shock leads were attached to the electrodes by removable connectors.

The restraint tube was made from .5 cm clear plastic stock and was 23 cm long and 10 cm in diameter. A horizontal floor was created by gluing a clear plastic plate (6 cm x 23 cm x .5 cm) onto the ventral surface of the tube's interior. A hole, 2.8 cm x 3 cm, cut in both the floor and the tube at the extreme posterior end allowed feces to fall free. A longitudinal slit, 2.5 cm wide, ran the entire length of the tube's dorsal surface to allow for "threading" of the animal's tail. This opening was covered during the session by a plastic cover that fit snugly. The posterior end of the tube was permanently closed by a clear plastic plate (12 cm x 15 cm x .5 cm). This plate had a vertical slit, 3 cm wide, that allowed the rat's tail to extend outside of the tube where it could be secured to a plastic bar by cloth-backed surgical tape.

Once the animal was "threaded" into the tube and its tail secured, a 12.5 cm x 17 cm x 2.5 cm plastic cap, to which the manipulandum was attached, was affixed to the anterior end of the tube. The manipulandum was a .5 cm thick clear plastic plate hinged to the cap at the level of the restraint tube floor. The plate was 8 cm in diameter and closely fit the interior of the tube. A single hole was cut in the center of the plate (1.5 cm x 2.2 cm) to allow for the insertion of a second manipulandum if desired. The manipulandum was hinged so that it hung into the tube at an angle of 10 degrees from
the vertical. The animal could use his nose to displace this plate. Such a displacement closed a microswitch and was counted as a response. Approximately .30 Newtons of force were required to close the microswitch.

The experimental sessions were conducted in three force-ventilated experimental chambers into which the entire apparatus was placed. Each chamber was equipped with a viewing window and a 40-watt incandescent house light. White noise was provided by a Model 901A Grason-Stadler Noise Generator (Grason-Stadler, West Concord, Massachusetts). The white noise and the ventilating fan combined to produce approximately 80db of masking noise within the chamber.

Electromechanical equipment was used for schedule control and data collection. Responses were also monitored by cumulative recorders (Gerbrands, Arlington, Massachusetts). Shocks were generated by Model 700 Grason-Stadler Shock Generators.

Procedure

Experimental sessions were conducted 5 days each week. Two groups of three rats were used. Each group received a 2 milliampers shock every 3.5 minutes. There were 16 shocks each session, and sessions lasted 59.5 minutes. For one group (Fixed-time group), responses had no effect; these animals received .5 seconds of shock every 3.5 minutes regardless of their behavior. For the other group (Escape group), a response in the presence of a shock terminated that shock. All other responses had no programmed consequences.
All animals in each group were prepared similarly and tested simultaneously. The animals were removed from their home cages and individually "threaded" into a restraint tube. The distal portion of the tail was secured with cloth-backed surgical tape to the plastic bar (as described previously), and the cap was attached to the anterior end of the tube. The cap and tube were then snapped onto the baseplate. Each animal's tail was cleansed with isopropyl alcohol and Electro-Sol EKG Cream (Scientific Instruments, Rochester, New York) was rubbed into the skin at the electrode site. The cream was used to prevent skin damage and reduce skin electrical resistance. The electrodes then swung into position and the resistance through the tail was measured across the two electrodes. If the tail resistance was not in the range of 10,000 to 20,000 ohms, more EKG cream was applied and rubbed into the tail. This procedure was repeated until the resistance was within the above range. The entire apparatus was then placed into the chamber. After this, the experimenter initiated the session at which time house lights, white noise, control equipment, and recording devices were activated simultaneously. The session was terminated automatically 3.5 minutes after the 16th shock.

Immediately after the session terminated, the subjects were removed from the chamber and the tail resistances were again measured and recorded. Following each session, the subjects' tails were cleansed with isopropyl alcohol, the tubes were thoroughly washed with soap and water, and the manipulandum was wiped with isopropyl alcohol.
Since certain characteristic response patterns seen on fixed-time schedules with shock appear to develop slowly (Hutchinson, 1977), a baseline of approximately 90 sessions preceded drug administration for both groups.

The data collected during each session included total responses, post-shock response latencies, and responses occurring during the first 5 seconds after each shock. Additionally, each shock-shock interval was divided into 7 30-second bins, and responses occurring in each bin were accumulated throughout the session. The temporal locations of responses within the intervals were also assessed visually by inspection of the cumulative record.

Drug Preparation and Schedule of Administration

Chlorpromazine hydrochloride was purchased as Thorazine (Smith, Kline, & French Corporation, Philadelphia, Pennsylvania) from the Veratex Corporation, Troy, Michigan. To reduce measurement error, the commercially available concentration of 25 mg/ml was decreased to 12.5 mg/ml by mixing the CPZ with an equal amount of physiological saline (0.9%). This solution was prepared weekly. All injections were given subcutaneously. Four doses of CPZ were given: 1 mg/kg, 2 mg/kg, 3 mg/kg, and 4 mg/kg. Since the actual volume of CPZ given only varied from .06 ml to .21 ml, no attempt was made to equalize volumes across dosages. All saline injections were 0.2 ml.

Chlorpromazine was usually given on Wednesday of each week, 30 minutes before the session began. Saline injections were given 30 minutes pre-session on all other days. Sessions on Mondays and
Tuesdays served as baseline for the particular dosage level given each animal on Wednesday. Dosages were given in a counterbalanced order fully described in Table 1. Each does was given to each animal twice.
# TABLE 1

Order of Drug Administration

<table>
<thead>
<tr>
<th>Group</th>
<th>Subject #</th>
<th>Dose in mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed-time</td>
<td>F1</td>
<td>1 3 2 1 4 3 2 4</td>
</tr>
<tr>
<td>Fixed-time</td>
<td>F2</td>
<td>4 2 3 4 1 2 3 1</td>
</tr>
<tr>
<td>Fixed-time</td>
<td>F3</td>
<td>3 1 4 3 2 1 4 2</td>
</tr>
<tr>
<td>Escape</td>
<td>E1</td>
<td>1 4 3 2 1 4 3 2</td>
</tr>
<tr>
<td>Escape</td>
<td>E2</td>
<td>4 1 2 3 4 1 2 3</td>
</tr>
<tr>
<td>Escape</td>
<td>E3</td>
<td>3 2 1 4 3 2 1 4</td>
</tr>
</tbody>
</table>
RESULTS

Chlorpromazine reduced total nose press responses for all animals at all dose levels. Total responses per session for Baseline and all drug doses are given along with summary data in Table 2. Baseline rates are averages of the two sessions prior to drug administration. Mean response rate per session across doses for each group is shown in Figure 2. As can be seen, the fixed-time schedule (FT) generated more responding than did the escape schedule (ESC). Also, chlorpromazine (CPZ) decreased the response rate under the fixed-time schedule to a greater degree and in a more orderly fashion across doses. Figure 3 expresses this relationship as a percentage of Baseline response rate per session, across doses. For the FT group, mean rates were decreased to 72.0%, 37.5%, 33.3%, and 26.2% of Baseline at CPZ doses of 1 mg/kg, 2 mg/kg, 3 mg/kg, and 4 mg/kg, respectively. Mean ESC group rates were decreased to 60.3%, 62.8%, 46.0%, and 46.2% of Baseline at the same respective doses. Mean response rates at each dose level are shown for individual subjects in Figure 4 for both groups. The magnitude of the change from Baseline due to CPZ appears to be a function of the absolute rate of response in the Baseline condition.

Since total rate was decreased at all doses, a change in the distribution of responses within shock-shock intervals is best expressed, for each 30 second bin, as a percentage of the total rate. In this way, a shift in response distribution due to CPZ

16
TABLE 2

Individual and Group Mean Response Rates Across Doses of CPZ

<table>
<thead>
<tr>
<th>Subject Schedule</th>
<th>Administration</th>
<th>1 mg/kg</th>
<th>2 mg/kg</th>
<th>3 mg/kg</th>
<th>4 kg/mg</th>
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</thead>
<tbody>
<tr>
<td>Fixed-time</td>
<td></td>
<td>Base</td>
<td>CPZ</td>
<td>Base</td>
<td>CPZ</td>
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<tr>
<td>F1</td>
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<td>113</td>
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<td>2</td>
<td>177</td>
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<tr>
<td>Fixed-time</td>
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<td>186</td>
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<td></td>
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<td>84</td>
<td>117</td>
<td>61</td>
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<tr>
<td></td>
<td>2</td>
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<td>86</td>
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<tr>
<td>MEAN</td>
<td></td>
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<td>85</td>
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<td>EL</td>
<td></td>
<td>100</td>
<td>52</td>
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<td>75</td>
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<tr>
<td>Escape</td>
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<td>175</td>
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<td>24</td>
<td>24</td>
<td>18</td>
</tr>
<tr>
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</tr>
<tr>
<td>E3</td>
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<td>94</td>
<td>54</td>
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<td>35</td>
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<tr>
<td>Escape</td>
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<td>75</td>
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<tr>
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<td></td>
<td>90</td>
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<td>78.5</td>
<td>29.5</td>
</tr>
<tr>
<td>GROUP MEAN</td>
<td></td>
<td>88.5</td>
<td>47</td>
<td>88.6</td>
<td>48.3</td>
</tr>
</tbody>
</table>

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FIGURE 3

[Graph showing data points and lines representing ESCAPE and FIXED-TIME against CHLORPROMAZINE (mg/kg).]

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FIGURE 4

CHLORPROMAZINE mg/kg

MEAN RESPONSES PER SESSION
can be assessed even though the total rates for CPZ are reduced compared to Baseline. Mean Baseline rates and mean drug rates, across 30 bins, are shown in Table 3 as a percentage of total responses. Data from Table 3 are expressed graphically in Figure 5, for both groups. As can be seen from Figure 5, the distribution of responses within the shock-shock interval was little affected at any dose of CPZ. Chlorpromazine appeared to slightly increase the probability of a response in the immediate post-shock period (Bin 1) for both groups. The percentage of responses occurring in the immediate pre-shock period (Bin 7) was not increased at any dose. At the highest dose, responding in the pre-shock period was completely eliminated. Figure 6 shows the cumulative record of Subjects F1 and F3 for both a drug and a Baseline session. Note especially the lack of responses in the pre-shock period.

Post-shock response bursts were defined as responses that occurred during the 5 second period following shock offset. The mean number of responses emitted as bursts were decreased with respect to mean Baseline bursts across all doses for both groups (Figure 7). This effect closely parallels the overall rate decreasing effect of CPZ (Figure 3). Figure 8 shows mean bursts expressed as a percentage of total responses. Although there was not a significant difference between the individual Baseline and drug effect response burst means (correlated, two-tailed rank sign difference test), the group mean rates do show a slightly greater percentage of responses being emitted as bursts in the drug condition.
<table>
<thead>
<tr>
<th>Group and Dose</th>
<th>Mean Percent of Total Responses</th>
<th>Mean Percent of Total Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Fixed-time</strong></td>
<td></td>
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</tr>
<tr>
<td>1 mg/kg</td>
<td>64.0</td>
<td>12.0</td>
</tr>
<tr>
<td>2 mg/kg</td>
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</tr>
<tr>
<td>1 mg/kg</td>
<td>67.8</td>
<td>14.8</td>
</tr>
<tr>
<td>2 mg/kg</td>
<td>60.7</td>
<td>14.8</td>
</tr>
<tr>
<td>3 mg/kg</td>
<td>61.3</td>
<td>11.0</td>
</tr>
<tr>
<td>Escape</td>
<td>60.3</td>
<td>12.0</td>
</tr>
</tbody>
</table>
FIGURE 6

Baseline

3.5 MINUTES

F1
CPZ 1 mg/kg

E3
Baseline

E3
CPZ 1 mg/kg

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FIGURE 7

[Graph showing data for ESCAPE and FIXED-TIME with chlorpromazine concentrations on the y-axis and sessions on the x-axis.]

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FIGURE 8

ESCAPE

• BASELINE

★ CPZ

FIXED-TIME

EMITTED AS BURSTS PER SESSION

PERCENT OF TOTAL RESPONSES

CHLORPROMAZINE

mg/kg

1 2 3 4

1 2 3 4
Table 4 shows the effect of chlorpromazine on mean post-shock response latencies. Baseline latencies for the fixed-time group (FT) were larger than those of the escape group (ESC) by approximately a factor of 10. Also, mean Baseline latencies are more variable for the FT group than for the ESC group. The mean latencies were increased for both groups at all doses of CPZ. Latencies for the FT group were more greatly affected by CPZ than were latencies for the ESC group.
## TABLE 4

Mean Post-Shock Response Latencies

<table>
<thead>
<tr>
<th>Group and Dose</th>
<th>Baseline (Seconds)</th>
<th>Drug (Seconds)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed-time 1 mg/kg</td>
<td>0.90</td>
<td>4.56</td>
</tr>
<tr>
<td>Fixed-time 2 mg/kg</td>
<td>1.87</td>
<td>36.57</td>
</tr>
<tr>
<td>Fixed-time 3 mg/kg</td>
<td>1.39</td>
<td>56.64</td>
</tr>
<tr>
<td>Fixed-time 4 mg/kg</td>
<td>2.33</td>
<td>33.28</td>
</tr>
<tr>
<td>Escape 1 mg/kg</td>
<td>0.17</td>
<td>0.27</td>
</tr>
<tr>
<td>Escape 2 mg/kg</td>
<td>0.20</td>
<td>0.31</td>
</tr>
<tr>
<td>Escape 3 mg/kg</td>
<td>0.26</td>
<td>0.70</td>
</tr>
<tr>
<td>Escape 4 mg/kg</td>
<td>0.19</td>
<td>0.36</td>
</tr>
</tbody>
</table>

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DISCUSSION

A comparison of Baseline rates of responding between the fixed-time group and the escape group shows several similarities. Both schedules generated moderately high rates of responding, with the fixed-time shock schedule actually producing a higher rate. The temporal distribution of responses within the shock-shock interval was almost identical for the two groups, as was the percentage of total responses emitted as bursts. These findings are in agreement with Hutchinson's contention that complex patterns of responding can be produced as a direct result of the response-independent presentation of an aversive event, and that these patterns can resemble those produced under response-dependent schedules (Hutchinson, 1977). The effect of the escape contingency in the present study is, however, shown in the actual number of responses emitted as bursts and in the shock-response latencies of the groups.

The overall rate-reducing effects of CPZ seen under fixed-time shock schedules are comparable to those typically observed under avoidance schedules in a variety of species (Fischman, et al., 1976; Hanson, et al., 1970; Stone, 1964). The rate reduction is, however, in contrast with the effects of CPZ reported for squirrel monkeys receiving fixed-time shock, where the response was pressing an ineffective lever (Emley & Hutchinson, 1972). In that study, overall response rates were increased by CPZ.
Several differences between Emley and Hutchinson's procedure and the present experiment's could account for this dissimilarity in drug effects. In addition to differences in species, apparatus, and response topography, the monkeys in the Emley and Hutchinson experiment had an alternative response option available (biting); this was not the case in the present study. Further, temporal patterns of responding differed in the two experiments. In their experiment, Emley and Hutchinson indicated that lever pressing occurred primarily in the pre-shock period and that CPZ acted upon this response class, increasing the rate. In the present study, Baseline rates were low in the immediate pre-shock period and CPZ had little effect on or decreased responding in this portion of the shock-shock interval. Thus, the present study does not suggest that CPZ increases anticipatory responding. However, the failure of rats to develop appreciable pre-shock responding during Baseline could have precluded the strengthening of this response class by CPZ. Also, several investigators (e.g., Latz, et al., 1969) have reported that a "freezing" response is likely in the pre-shock period. This freezing response may be of more strength and longer duration in the rat than in the squirrel monkey.

To clarify the possible role of the factors discussed above, studies using a variety of species and parameters would have to be undertaken. Through such studies, the importance of response topography, sequencial response patterning, and general species characteristics as determinants of drug effects on behaviors maintained under both response-independent and response-dependent schedules, might be discovered.
Chlorpromazine had little effect on the distribution of responses throughout the shock-shock interval. The slight increase seen in responding during the immediate post-shock period appears to be due to the relative insensitivity of responses educed as bursts to the rate-decreasing effects of CPZ. Although responses educed as bursts were decreased by CPZ at all doses, they were reduced proportionately less than were the total responses. Clark and Steele (1963) reported similar findings under avoidance schedules. The apparent insensitivity of the responses occurring as bursts may account for CPZ's "selective" ability to decrease avoidance responding at doses that do not affect escape. Clark and Steele argued that since post-shock bursts have little effect on the number of shocks delivered under avoidance schedules, but are crucial to effective escape, the relative insensitivity of this response class would make responding under escape schedules appear less sensitive to the disrupting effects of CPZ. Hutchinson (1977) likened responses that occur just after an aversive event to escape responses. The similarities between the two groups in rate of responses educed as bursts, as well as the effect of CPZ on this response class, support Hutchinson's analysis.

Many reports of responding under escape schedules only report whether or not a response occurs in the presence of the aversive stimulus. In the present study, responding occurred throughout the shock-shock interval and was decreased by CPZ. The decrease in overall response rate due to CPZ under the escape schedule is in agreement with results reported by Cook and Catania (1964) with squirrel monkeys under fixed-interval escape. However, total responses
under the escape schedule were reduced less, proportional to their baseline, than were total responses under the fixed-time schedule. That this difference between the groups is neither large nor totally consistent across doses suggests that the presentation of the shock itself exerts considerable control over behavior. Although CPZ increased shock-response latencies in both groups, the contingent relationship between a response and shock termination appears to have limited the magnitude of this increase in the escape group.

In summary, fixed-time delivery of shock was shown to generate behavior similar to that produced under an escape schedule in terms of rate and temporal distribution of responses emitted immediately after the shock and the shock-response latency were sensitive to the presence of the escape contingency. Chlorpromazine reduced the rate of responding in both groups, but had no differential effect across the groups on the temporal distribution of responses within the shock-shock interval. In contrast to early findings (Emley & Hutchinson, 1972), no evidence was found of an ability of CPZ to strengthen responses that occur just prior to the aversive event.


FIGURE CAPTIONS

Figure 1. Apparatus used in experiment.

Figure 2. Mean response rate per session across doses of CPZ. Baseline rates are means of the two sessions prior to each drug administration.

Figure 3. Mean response rate per session as a percentage of baseline across doses of CPZ.

Figure 4. Individual mean response rates across doses of CPZ. Baseline rates are means of the two sessions prior to each drug administration.

Figure 5. Individual mean response rates, as a percentage of total responses, across 30 second bins and doses of CPZ.

Figure 6. Drug and baseline session cumulative record for subjects Fl and E3.

Figure 7. Mean responses emitted as bursts for baseline sessions and all doses of CPZ.

Figure 8. Mean responses emitted as bursts expressed as a percentage of total responses per session