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Effect of Chlordiazepoxide on Schedule-Controlled Responding and Schedule-Induced Drinking[1]

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BACOTTI, A. V. AND J. E. BARRETT. *Effects of chlordiazepoxide on schedule-controlled responding and schedule-induced drinking.* PHARMAC. BIOCHEM. BEHAV. 4(3) 299–304, 1976. – Lever pressing of four rats was maintained under a multiple fixed ratio 80, fixed interval 2-min schedule of food presentation. Water was concurrently available from a drinking tube. Overall rates of lever pressing were highest under the fixed ratio schedule and, for three rats, most drinking occurred during the pause preceding responding under the fixed interval schedule. Chlordiazepoxide increased the lower rates of lever pressing maintained under the fixed interval schedule but generally decreased the higher response rates under the fixed ratio schedule. The effects of chlordiazepoxide on schedule-induced licking also depended on the extent to which this response occurred in each schedule component. Typically, chlordiazepoxide produced relatively greater increases in the lower levels of licking and either increased less or decreased licking in that component where, under control conditions, this response was more extensive. Chlordiazepoxide also produced overall increases in the total amount of water consumed during the session. When the number of food pellets obtained during the experimental session was given all at one time in the home cage, the amount of water ingested over a period of time equivalent to the session duration was substantially less than that consumed during the experimental session. Chlordiazepoxide did not increase home cage water consumption under this condition.

Chlordiazepoxide Multiple schedule Schedule-induced Drinking Rats

THE schedule under which reinforcing events are presented has often been shown to determine the pattern and rate of responding as well as the effects various drugs will have on behavior [6, 10, 13]. Additionally, under certain conditions, schedules of reinforcement will also frequently engender other behaviors such as excessive drinking [2, 7, 8] and attack or aggression [1,9]. This latter class of behaviors, often called schedule-induced, is characterized by its excessiveness and by its close proximity to the period immediately following food delivery [8].

A number of studies have compared the effects of various drugs on schedule-induced and schedule-controlled behavior [3, 7, 12, 14, 15]. For example, McKearney [12] compared the effects of methamphetamine and chlordiazepoxide on schedule-controlled and schedule-induced drinking. In that experiment, the first lick on a water filled drinking tube after 3 min had elapsed produced food (schedule-controlled licking); additionally, high rates of licking occurred immediately following food delivery (schedule-induced licking). Both chlordiazepoxide and methamphetamine had little effect on the rate of schedule-induced drinking, but rates of schedule-controlled licking were increased with chlordiazepoxide. Similarly, with squirrel monkeys, rates of lever pressing maintained under a fixed interval 3-min schedule were also increased with chlordiazepoxide, as was the amount of fluid (alcohol or water) consumed following food delivery [2].

The present experiment was designed to examine characteristics of schedule-induced drinking by rats when lever pressing was maintained under a multiple fixed interval, fixed ratio (multiple FI FR) schedule of food presentation. Depending on the parameter values employed, these schedules can control different rates and patterns of responding as well as different interreinforcement times and pause durations. The role of interreinforcement time has been widely implicated in the occurrence of schedule-induced behaviors [8,9]. In addition to assessing the development and maintenance of schedule-induced drinking under these conditions, the effects of chlordiazepoxide were also examined.

METHOD

Animals

Four naive rats of the Wistar strain, 8 months old at the start of the experiment, were maintained at 80% of their

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unrestricted feeding weights (range 268–330 g). Water was available at all times in the home cage.

Apparatus

A 23 cm × 20.5 cm × 19 cm experimental chamber constructed from aluminum and Plexiglas was placed in a sound attenuating enclosure. The front aluminum wall of the chamber contained two 6-W lights mounted above a lever (R. Gerbrands Co.) that required a force of 0.22 N to operate controlling equipment and record as a response. A 2-W light was mounted on the rear aluminum wall. Food (45 mg Noyes pellets) was delivered into a food cup situated to the left of the lever. A 2.5 cm × 1 cm opening in the left Plexiglas wall was made 16.5 cm from the front of the chamber. A water bottle was mounted behind this opening. Contacts on the drinking tube were sensed by a drinkometer circuit. The enclosure and chamber were placed in a room supplied with white noise.

Procedure

Training. All rats were trained initially to press the lever by the method of successive approximations. Following this initial training, all rats were exposed to gradually increasing values of the multiple FR FI schedule. The final schedule consisted of a multiple FR 80, FI 2-min schedule. Under this procedure food was delivered after the 80th response (FR 80) or following the first response after a 2-min interval had elapsed (FI 2 min). During the FR component the chamber was illuminated by the 2 front lights and the rear light, whereas during the FI component only the rear light in the chamber was illuminated. Reinforcement consisted of the delivery of one 45 mg Noyes rat pellet at the end of each schedule component. Experimental sessions were conducted daily and consisted of 30 presentations of each schedule which alternated successively beginning with the FR. Rats 69, 70, and 73 were removed from the chamber after each session; Rat 74 remained in the chamber overnight.

Drug administration. Chlordiazepoxide was first administered after 24 sessions under the multiple FR 80 FI 2-min schedule. Each rat received at least two IP administrations of each dose (1.0, 3.0, 5.6 and 10.0 mg/kg) in an irregular order 30 min before the start of a session. Doses are expressed in terms of the total salt. The drug was dissolved in physiological saline and administered in a volume of 1.0 ml/kg of body weight. A minimum of two sessions during which lever pressing and drinking returned to control levels was required between the administration of each dose. The number of sessions intervening between drug administrations was typically greater.

The effects of chlordiazepoxide on home-cage water consumption were determined as follows. On two separate occasions each rat received the 60 pellets that were normally obtained during the approximately 90 min session. These pellets were given all at one time in the home cage and the amount of water consumed during the period equivalent to that rat's session duration was determined. On subsequent days, injections of chlordiazepoxide were given, and, 30 min later, 60 pellets were placed in the cage. The amount of water consumed during this time was then compared with that on nondrug days. In this manner, it was possible to assess the amount of drinking that occurred when equivalent amounts of food were given on a non-intermittent basis. Furthermore, this procedure permitted a baseline against which to assess the effects of chlordiazepoxide on the quantity of drinking per se, independent of the schedules of food presentation. This phase of the study was conducted after the dose effect curves were obtained under the multiple schedule.

RESULTS

Control Performances

Overall response rates were highest under the FR component of the multiple schedule for all rats. FR responding, once initiated, generally occurred at a reasonably high steady rate until food was delivered. Under the FI schedule, a steady lower rate of responding typically occurred following a pause early in the interval. These control patterns of lever pressing are shown for two rats in the cumulative response records in Fig. 1.

Under nondrug conditions, most drinking occurred during the longer pause under the FI schedule. For rat R-69, however drinking usually occurred during the pause preceding the initiation of lever pressing under the FR schedule. Drinking for all rats was characteristically post-pellet and occurred at a high sustained rate. Figure 1 shows cumulative records depicting schedule-induced drinking for two rats, the one that drank predominately during the FR schedule (R-69) and one of those that drank during the FI schedule (R-70).

Average responses per minute and licks per pellet during each component of the multiple schedule are presented in Table 1 along with the average total water intake (ml) during the experimental sessions. The control data represent the average of all sessions (approximately 10, including saline controls) which immediately preceded the day on which the drug was administered. The drug data are based on the average of at least two administrations of each dose of chlordiazepoxide.

Effects of Chlordiazepoxide

Figure 2 shows the effects of chlordiazepoxide on lever pressing under the FR and FI schedules. The effects of each dose of chlordiazepoxide are expressed as percent changes in average control response rate. The relatively lower overall rates of responding under the FI schedule were increased at all but the highest dose (10.0 mg/kg) which decreased responding with R-69 and R-70. Lever pressing under the FR schedule was only slightly affected at lower doses (1.0–3.0 mg/kg) and was generally decreased at 5.6 and 10.0 mg/kg. Doses of chlordiazepoxide that either decreased or left unchanged the higher rates of FR responding, typically increased substantially the lower response rates maintained under the FI schedule.

Figure 3 shows percent changes in licks per pellet with chlordiazepoxide during each component of the multiple schedule. As shown in Table 1, licking differed for each rat both in terms of absolute magnitude and with regard to the component in which licking predominantly occurred. For R-69, substantially more licking occurred during the FR schedule. With chlordiazepoxide, licking by R-69 during the FR component was largely unchanged, whereas the less frequent licking during the FI schedule was increased markedly. For R-70 and R-74 licking occurred to a greater extent during the FI schedule. With R-70, at lower doses of chlordiazepoxide (1.0–3.0 mg/kg), licking during the FR

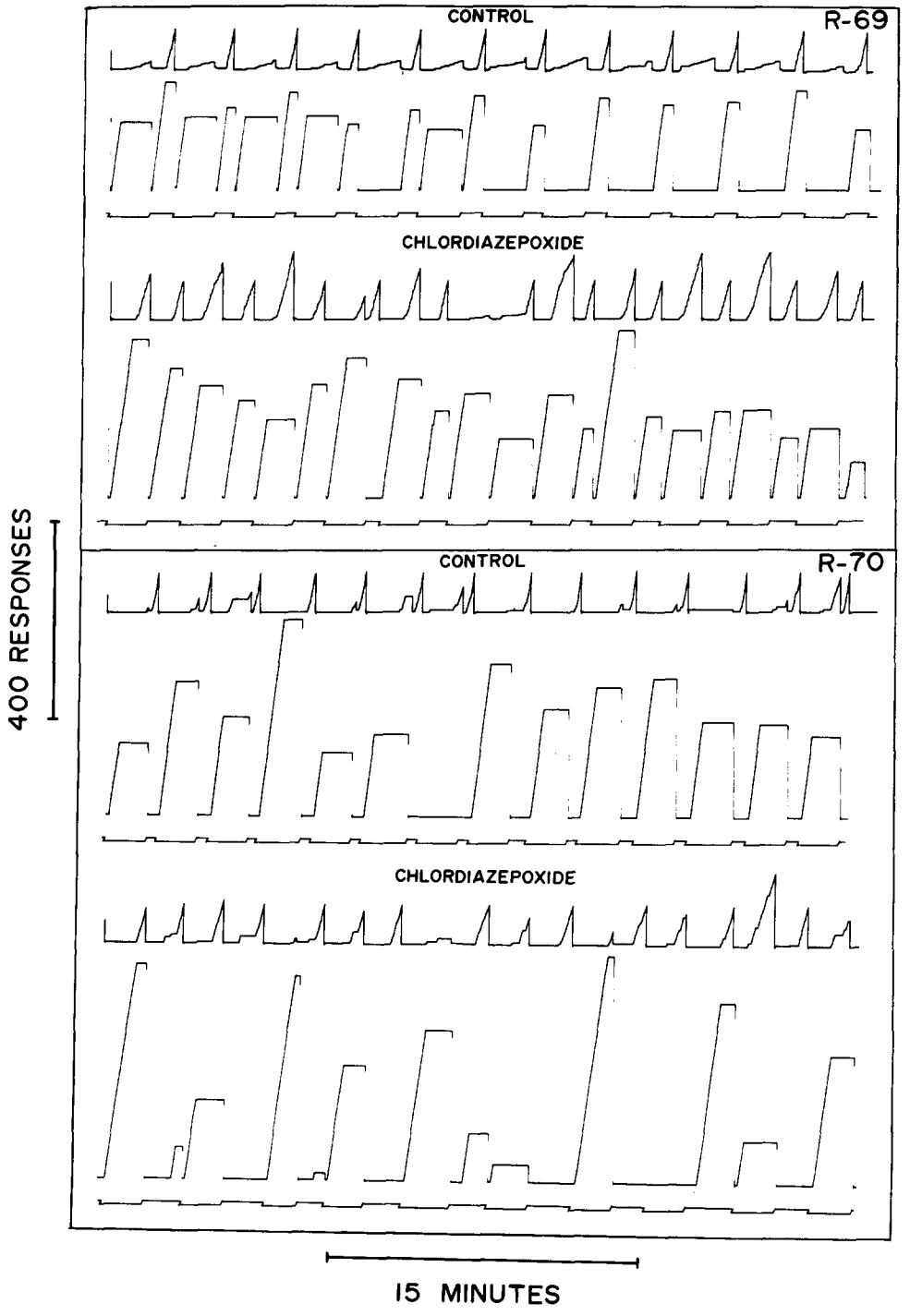

FIG. 1. Cumulative response records of two rats (R-69, R-70) showing patterns of lever pressing and licking under the multiple FR 80 FI 2 min food presentation schedule. Control records were taken from nondrug sessions on the day preceding those sessions in which 5.6 mg/kg chlordiazepoxide was administered. The upper record of each pair shows lever pressing and the lower record depicts licking responses on the water tube. The event line beneath each pair of records was deflected down during the FI schedule. Response pens reset to baseline following each pellet delivery. Note that for R-69, drinking later in the session typically occurred during the pause preceding responding under the FR schedule. R-70 typically drank during the pause occurring under the FI schedule. Ordinate: cumulative responses; Abscissa; time.

TABLE 1

ABSOLUTE RESPONSE RATES, LICKS PER PELLET AND ml WATER CONSUMED UNDER THE MULTIPLE SCHEDULE*

Animal	Dose (mg/kg)	Response Rate (R/min) FR	FI	Licks/Pellet FR	FI	Ml H_2O (Session)
	Control	70.74	12.96	154.73	41.62	23.50
	S.E.M.	± 2.36	± 0.74	± 3.39	± 3.10	± 2.10
69	1.0	69.38	14.58	157.72	76.78	29.50
	3.0	72.26	14.58	159.24	84.12	34.00
	5.6	51.65	26.72	173.22	125.41	37.00
	10.0	0.00	0.00	0.00	0.00	0.00
	Control	95.00	10.23	13.76	111.45	20.20
	S.E.M.	± 5.54	± 0.74	± 2.10	± 19.29	± 1.19
70	1.0	118.85	13.37	5.76	119.73	15.00
	3.0	94.78	13.17	6.10	174.94	27.00
	5.6	47.93	32.99	25.99	149.30	27.33
	10.0	0.00	0.00	0.00	0.00	0.00
	Control	34.18	7.62	102.95	176.35	30.75
	S.E.M.	± 2.28	± 0.55	± 20.05	± 20.23	± 2.64
73	1.0	47.48	9.86	112.33	151.72	34.00
	3.0	33.05	12.46	85.98	132.20	28.50
	5.6	45.52	14.88	117.31	223.33	44.50
	10.0	11.35	10.03	84.07	88.60	21.00
	Control	42.56	10.03	56.30	370.51	48.11
	S.E.M.	± 3.50	± 1.18	± 7.95	± 19.55	± 2.52
74	1.0	44.27	11.65	75.72	350.72	53.00
	3.0	46.83	17.22	85.59	345.38	50.00
	5.6	28.52	19.50	87.11	280.60	46.33
	10.0	2.50	24.07	160.67	222.75	37.00

*†Control performances are based on at least 8 nondrug and 2 saline control sessions; drug data based on at least 2 determinations at each dose.

was decreased and licking under the FI schedule was increased. At 5.6 mg/kg the percent increase in licking during the FR was greater than that which occurred in the FI schedule. For R-74, the more frequent licking during the FI was decreased at all doses, whereas less frequent licking in the FR schedule was substantially increased. Licking for R-73 in each of the components was more nearly equal under control conditions than was the case with other rats and, except at the 10.0 mg/kg dose, was generally unchanged with chlordiazepoxide. These changes in rates and patterns of lever pressing and drinking with 5.6 mg/kg chlordiazepoxide are also shown for rats R-69 and R-70 in Fig. 1. Particularly noteworthy in these records are the marked and consistent increases with chlordiazepoxide in licking under the FI schedule for R-69.

Figure 4 presents percent changes in total fluid intake at each dose of chlordiazepoxide. All rats showed increases in fluid consumption, although these effects were somewhat less for R-74 who remained in the chamber overnight. The amount of drinking under control conditions as well as amounts obtained with chlordiazepoxide may have been affected by the fact that fluid consumption could occur over longer periods of time. With the exception of R-74, however, most doses of chlordiazepoxide produced sizeable increases in fluid intake except at 10.0 mg/kg which decreased this measure. The decrease in fluid intake at the 10.0 mg/kg dose may have been more directly related to the decrease in pellet deliveries stemming from the overall lowered rate of responding.

The effects of feeding the session equivalent of 60 pellets all at one time in the home case and measuring water intake with and without 5.6 mg/kg chloridazepoxide are presented in Table 2. The amount of water consumed during a period of time equivalent to an experimental session was substantially less when the 60 pellets were given all at once (see Table 1). During a comparable period of time the rats in this experiment typically drank 3 to 5 times more water when food was delivered intermittently during the session. Further, chlordiazepoxide did not increase the amount of water consumed under the homecage feeding condition. Except for R-73, where drinking was increased, overall water intake decreased with 5.6 mg/kg chlordiazepoxide. This dose produced maximal increases in water intake during the session.

DISCUSSION

Drinking occurred when lever pressing by rats was maintained under a multiple FR FI schedule of food presentation. As in previous reports [2, 8, 14, 15], this drinking was typical of that described as being schedule-induced; it was confined to the period immediately following pellet delivery and it was excessive relative to that occurring during a comparable time period with an equivalent amount

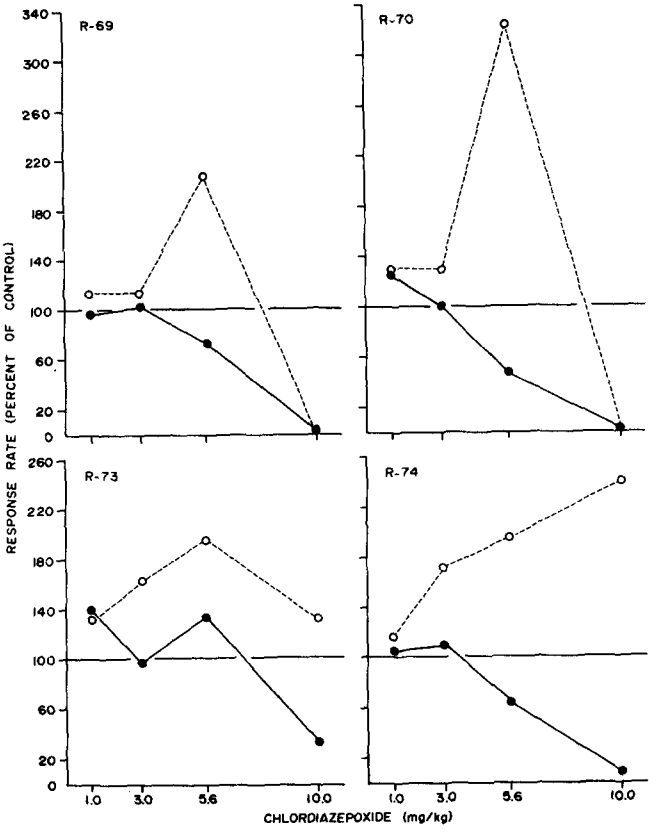

FIG. 2. Rates of lever pressing with each dose of chlordiazepoxide for all 4 rats. Changes in response rate are expressed as percent changes in control performance. The solid horizontal line indicates control performance. Open circles represent responding under the FI schedule, filled circles represent responding under the FR schedule.

TABLE 2

EFFECTS OF CHLORDIAZEPOXIDE (5.6 MG/KG) ON WATER INTAKE WITH 60 FOOD PELLETS GIVEN IN THE HOME CAGE

Animal	Ml water intake Control*	5.6 mg/kg CDAP*
R-69	9.0	6.5
R-70	6.5	5.0
R-73	3.5	7.5
R-74	4.0	2.0

*Mean of 2 determinations.

of pellets given nonintermittently. The precise temporal locus and extent of drinking, however, differed slightly among rats. Under control conditions most rats drank predominately during the pause which occurred under the FI schedule. With one rat (R-69) however, drinking usually occurred during the pause preceding responding under the FR schedule. The factors contributing to the relatively more excessive drinking during the FI schedule seem reasonably straightforward: food delivery is not postponed because the interval need be terminated by a single

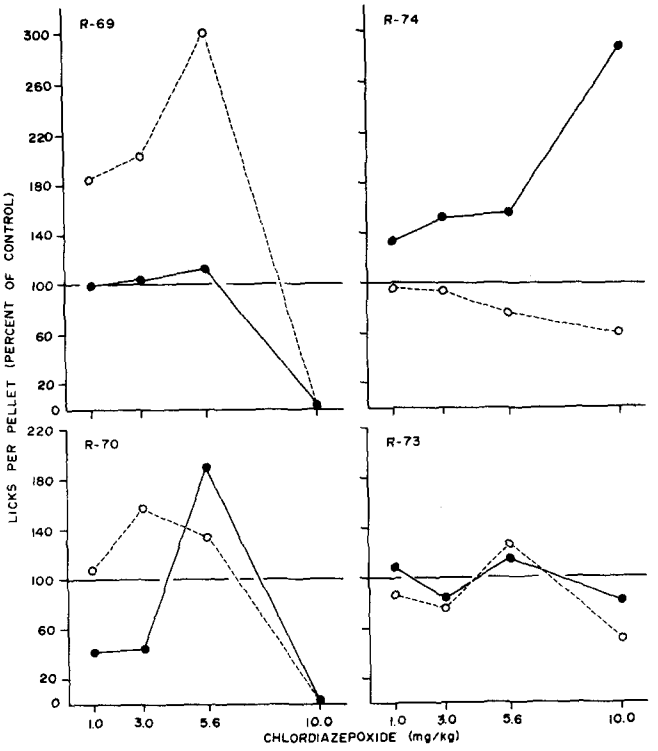

FIG. 3. Changes in licks per pellet with chlordiazepoxide as percent changes from control performance. Points above the horizontal line at 100 indicate increases in licking; points below the line represent decreases with chlordiazepoxide. Open circles represent licks per pellet under the FI schedule; filled circles represent licks per pellet under the FR schedule.

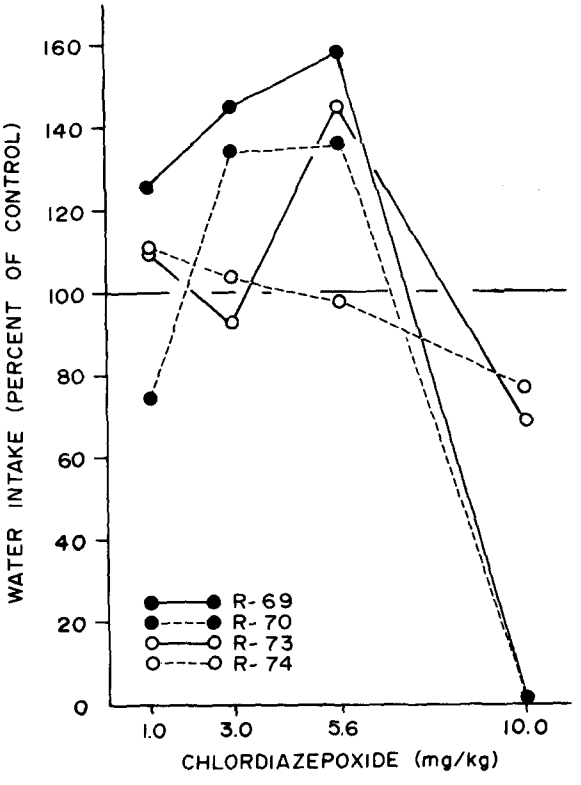

FIG. 4. Changes in water intake (ml) during the experimental session as the percent of control performance for all rats after chlordiazepoxide.

response; it is not likely, therefore, that interreinforcement time would be lengthened by long periods of drinking. Under the FR schedule, however, extensive drinking could increase the interreinforcement time. Although at present there is no basis to account for the difference in R-69 from the other rats, it would seem that the pattern and locus of drinking that developed with the other three rats would be more representative of drinking under this multiple FR FI schedule.

Chlordiazepoxide generally decreased the relatively higher rates of FR lever pressing at doses that increased the lower rates of responding maintained under the FI schedule. The effects of chlordiazepoxide on responding in this case are similar to those obtained with many other drugs in that the control response rate appears to be an important determinant of the effect a drug will have on behavior [4, 6, 10, 13]. Under multiple FR FI schedules, a wide variety of drugs have been shown to increase overall lower rates of FI responding at doses that produced decreases in higher rates of responding maintained under the FR schedule [5, 10, 13]. In the present study, the effects of chlordiazepoxide on lever responding were also rate dependent. Chlordiazepoxide also produced orderly effects on licking that depended on the frequency with which this behavior occurred; at a given dose of chlordiazepoxide, relatively less frequent licking was generally increased proportionally more than the licking that occurred with a higher frequency.

The increasing effects of chlordiazepoxide on overall water intake per session are comparable to those previously found with squirrel monkeys [2]. Although increases in fluid intake of fluid deprived rats have been obtained with chlordiazepoxide [11], this type of increase in fluid consumption cannot account for the results obtained in the present study. The increases in water intake reported here were not simply drug induced, in that chlordiazepoxide administered in the home cage with water available and an equivalent amount of food did not result in a comparable amount of water ingested. The effects of chlordiazepoxide on schedule-induced drinking and schedule-controlled lever pressing depended on the control of these behaviors by the schedule of food presentation.

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