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Stimulus Control by Diazepam of Behavior Maintained Under Fixed-Ratio Stimulus-Shock Termination Schedules in Rats

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SHANNON, H. E. *Stinulus control by diazepam of behavior maintained under fixed-ratio stimulus-shock termination schedules in rats.* PHARMACOL BIOCHEM BEHAV **20**(5) 715–720, 1984.—The stimulus control of behavior by diazepam (1.0 mg/kg) was investigated where responding was maintained under fixed-ratio (FR) schedules of stimulus-shock termination in rats. The size of the FR requirement was either 1, 5, 10, or 20 responses. At each FR requirement, dose-effect curves were determined for diazepam, flurazepam, pentobarbital and cyproheptadine. Diazepam-like discriminative stimuli were produced by flurazepam and pentobarbital but not by cyproheptadine. The magnitude of the FR requirement had no significant effect on the dose-effect curves for percentage of responses emitted on the diazepam-appropriate choice lever for any of the four drugs. On the other hand, the effects of these drugs on rates of responding depended on the magnitude of the FR requirement. None of the drugs altered response rates under the FR1 schedule. Diazepam tended to increase response rates under the FR5 schedule, but had no effect or decreased rates under the FR10 and FR20 schedules. Flurazepam and pentobarbital predominantly decreased rates at FR requirements of 5, 10 or 20 responses. Cyproheptadine had no significant effect on response rates at any schedule parameter. Together with previous reports, the present results indicate that the discriminative effects of diazepam are similar under schedules employing noxious (this study) or non-noxious (other reports) consequences, even though the effects on response rates of diazepam-like drugs differ depending on the schedule of reinforcement and consequent event maintaining the behavior.

Drug discrimination Benzodiazepines Pentobarbital Fixed-ratio schedules Stimulus-shock termination

NUMEROUS studies have used fixed-ratio (FR) schedules of food or water presentation as a behavioral baseline for evaluating the stimulus control of behavior by drugs (e.g., [3, 6, 12]). However, behavior maintained by food or water presentation may be disrupted or even abolished by relatively low drug doses; these disruptive effects may preclude testing a broad enough range of doses (cf., [4,22]). Schedules of stimulus-shock termination permit higher doses of drugs to be tested without suppression of responding. One purpose of the present studies was to investigate FR schedules of stimulus-shock termination in the rat as behavioral baselines for studying stimulus control by drugs. FR schedules have the advantage over previously used discrete-trial avoidance procedures (e.g., [21]) in that the effects of drugs on rates of FR responding can be directly compared to the extensive literature on the effects of drugs on schedule-controlled responding maintained by a variety of environmental events. Diazepam, which has been shown to function as a discriminative stimulus in rats responding under a FR10 schedule of food presentation [11] or under a discrete-trial schedule of stimulus-shock termination [23], was used as the training drug. Flurazepam and pentobarbital were also studied for purposes of comparison. Cyproheptadine, which has been shown to increase rates of punished responding in a manner similar to benzodiazepines [5], was included as an active control. In addition, the magnitude of the FR requirement was varied from one response to 5, 10 or 20 responses in order to determine whether the size of the FR requirement influences either the results of substitution tests, the effects of the drugs on rates of responding, or both.

METHOD

Subjects

The subjects were five Fischer-derived F344 male rats (Harlan Industries, Indianapolis, IN, USA) weighing 250 to 300 g at the start of discrimination training. Between experimental sessions, the rats were housed two or three per cage in a large colony room with food and water continuously available. The lights in the colony room were illuminated between 6:00 a.m. and 6:00 p.m.

Apparatus

Two-lever rat chambers (model 1101-L, Grason-Stadler Co., Inc., Bolton, MA, USA) were used. A clear Plexiglas partition separated the two response levers. A scrambled electric shock was delivered to the grid floor of the test

TABLE 1

ORDER IN WHICH RATIO REQUIREMENTS AND DRUGS WERE TESTED IN INDIVIDUAL RATS

Rat No.	Order	
53(38)*	FR10:	Diazepam, pentobarbital
	FR 5:	Diazepam, flurazepam, pentobarbital, cyproheptadine
	FR20:	Diazepam, pentobarbital
	FR 1:	Diazepam, flurazepam, pentobarbital, cyproheptadine
57(48)	FR 1:	Diazepam, pentobarbital, flurazepam, cyproheptadine
	FR10:	Diazepam, flurazepam, pentobarbital, cyproheptadine
	FR 5:	Diazepam, flurazepam, pentobarbital, cyproheptadine
	FR20:	Diazepam, pentobarbital, flurazepam, cyproheptadine
58(28)	FR10:	Diazepam, pentobarbital, flurazepam, cyproheptadine
	FR20:	Diazepam, flurazepam
	FR 1:	Diazepam, pentobarbital, flurazepam, cyproheptadine
	FR 5:	Diazepam, flurazepam, pentobarbital, cyproheptadine
67(42)	FR 5:	Diazepam, pentobarbital, flurazepam, cyproheptadine
	FR 1:	Diazepam, flurazepam, pentobarbital, cyproheptadine
	FR20:	Diazepam, flurazepam, pentobarbital
	FR10:	Diazepam, pentobarbital, flurazepam, cyproheptadine
68(32)	FR 5:	Diazepam, pentobarbital, flurazepam, cyproheptadine
	FR10:	Diazepam, flurazepam, pentobarbital, cyproheptadine
	FR 1:	Diazepam, pentobarbital, flurazepam, cyproheptadine
	FR20:	Diazepam, flurazepam, pentobarbital, cyproheptadine

*Number in parentheses indicates the number of sessions required to meet the discrimination training criterion of 8 consecutive sessions where responding was at least 95 percent correct.

chamber by a constant current shock generator (model 700, Grason-Stadler Co., Inc.). The test chamber was enclosed in a light- and sound-attenuating, ventilated enclosure. White noise was presented continuously throughout the session. Schedule contingencies were programmed and data recorded by a SCAT 3002/PDP8 system (BKP Scientific, Berlin, MA, USA).

Discrimination Training

The rats were trained under a FR schedule of stimulus-shock termination to respond on one lever after an injection of saline and on the other lever after an injection of 1.0 mg/kg of diazepam. In the presence of the houselight, the rats were required to emit 1, 5, 10 or 20 consecutive responses on the lever appropriate for the presession injection in order to terminate the houselight and shock presentation. Beginning 4.0 sec after the illumination of the houselight, shock (1.0 mA) was presented as 1.0-sec pulses with 4.0 sec between pulses until the consecutive response requirement was met. Completion of the response requirement immediately extinguished the houselight, terminated shock presentation and initiated a 45-sec timeout period during which the chamber was dimly illuminated by a red stimulus light. Responses on the inappropriate choice lever reset the ratio requirement. Sessions ended after 20 or 10 (under the FR20 schedule) fixed-ratio components or 30 min, whichever occurred first. Sessions were ended after 10 components under the FR20 schedule because with longer sessions behavior was not well maintained and animals typically completed no more than 15 components during the 30-min session.

Training was initiated in all rats under an FR1 schedule of stimulus-shock termination. During the first two training sessions, a response on either choice lever terminated the stimulus-shock complex. Response shaping by reinforcing successive approximations of lever pressing was not required during these sessions. During the next two sessions, only responses on the drug-appropriate lever were reinforced although no injections were given. Only responses on the saline-appropriate lever were reinforced during sessions five and six. Beginning with session seven, diazepam (1.0 mg/kg) or saline was administered SC 30 min before each session on a double alternation basis and where only responses on the choice lever appropriate for the presession injection were reinforced. For rat 57, the FR requirement remained 1 response. The FR requirement was increased by 1 response every fourth session to an FR value of 5 for rats 53, 58, 67 and 68. The FR requirement was then increased to FR10 four sessions later for rats 53 and 58.

Training sessions were conducted 6 days/week until the rats completed at least 95 percent of the total responses under their respective FR requirements on the appropriate choice lever during eight consecutive sessions. The next two sessions (one diazepam and one saline) were conducted as test sessions under nondifferential reinforcement of choice responding (i.e., completion of the consecutive response requirement on either choice lever terminated a trial). A rat was considered to have acquired the discrimination if at least 95 percent of the responses during both test sessions were completed on the choice lever appropriate for the pretreatment injection. After the rats had met this criterion for acquisition of the discrimination, training sessions continued to be conducted on the first, second, fourth and fifth sessions of each week in order to maintain discrimination performance

at criterion levels. Saline and diazepam were administered on a double alternation basis across training sessions. A test session where 1, 5, 10 or 20 (as appropriate) consecutive responses on *either* lever could terminate the stimulus-shock complex was conducted on the third and sixth sessions of each week if the rat completed at least 95 percent of the total responses on the appropriate choice lever during the previous two training sessions.

In each rat, the FR values were studied in a different order (Table 1). At each FR value, dose-effect curves were determined first for diazepam, then for pentobarbital and flurazepam in random order, and lastly for cyproheptadine. After each dose-effect curve was determined at a given FR value, the FR value was changed. Decreases in the FR value were made abruptly; increases were made in increments to the next higher multiple of five responses every fourth session until the next final FR value was reached. Behavior was allowed to stabilize at the next FR value for 10 training sessions before determination of the next series of dose-effect curves. In some rats, behavior was not well maintained under the FR10 and FR20 schedules. In these rats, response rates declined after the determination of two or three dose-effect curves (Table 1) such that the animals were completing approximately half of the ratio components during either drug or saline training sessions or both. When this occurred, the ratio requirement was decreased to five responses until the rats were again completing all 20 ratio components during both drug and saline training sessions. The schedule was then changed (if required) to the next FR requirement.

Drugs

Diazepam and flurazepam diHCl were generous gifts from Hoffmann-LaRoche, Inc., Nutley, NJ, USA. Na pentobarbital was purchased from Abbott Laboratories, N. Chicago, IL, USA, and cyproheptadine was purchased from Merck, Sharpe and Dohme, W. Point, PA, USA. Diazepam was dissolved in saline adjusted to pH 1.5. Flurazepam was dissolved in distilled water. Na pentobarbital was dissolved in saline at pH 11. Cyproheptadine was dissolved in 60 percent (v/v) propyleneglycol and distilled water. All doses are expressed as the free drug. All drugs and drug vehicles were injected SC or IP in a volume of 1.0 to 3.0 ml/kg, 30 min before the start of a test session.

Data Analysis

Discrimination data are expressed as the percentage of the total reponses emitted on the diazepam-appropriate choice lever. Overall rates of responding were calculated by dividing the total number of responses by the total time in the presence of the houselight. Local rates of responding for FR values greater than 1 were calculated by dividing the total number of responses by the total time minus the total pause time preceding the first response of the ratio. The significance of differences among means within dose-effect curves was determined by analysis of variance and orthogonal comparisons [25]. Other comparisons were made using Student's *t*-test for paired comparisons.

RESULTS

Diazepam

At all FR values, diazepam occasioned dose-related increases in the percentage of responses emitted on the diazepam-appropriate choice lever (Fig. 1, left panel). Vehicle and the lowest dose of diazepam (0.1 mg/kg) occasioned greater than 95 percent responding on the saline-appropriate lever. A dose of 0.3 mg/kg of diazepam occasioned between 9 and 33 percent responding on the diazepam-appropriate lever. Doses of 1.0 and 3.0 mg/kg of diazepam occasioned greater than 98 percent diazepam-appropriate responding. These dose-effect curves for stimulus control of behavior at the different FR values were not significantly different from each other.

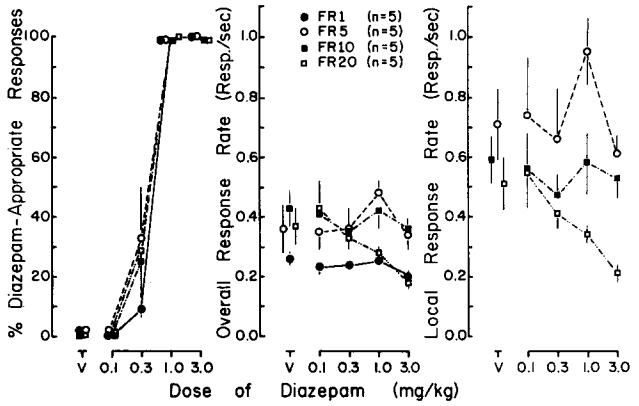

FIG. 1. Dose-effect curves for diazepam in rats trained to discriminate between saline and 1.0 mg/kg of diazepam under fixed-ratio (FR) schedules of stimulus-shock termination. Each point is the mean of one observation in each of the rats (n=number of rats). Abscissa: dose of diazepam in mg/kg on a log scale (V, vehicle). Ordinates: left panel, mean percentage of total responses emitted on the diazepam-appropriate choice lever; middle panel, mean overall response rates in responses/s; right panel, mean local response rates in responses/s. Vertical lines represent ±SEM and are absent when this value is less than the size of the point.

The effects of diazepam on overall rates of responding were dependent upon the ratio requirement (Fig. 1, middle panel). Vehicle control values under the FR1 schedule were approximately 0.26 responses/sec, indicating that the animals typically waited the 4.0 sec until the first shock onset to respond. Vehicle control rates ranged from approximately 0.36 to 0.43 responses/sec under the 5, 10 and 20 FR requirements. The control overall response rate was significantly lower under the FR1 schedule as compared to control rates under the other three ratio values. Overall response rates were not significantly altered by diazepam under the FR1, FR5 and FR10 schedules. Under the FR20 schedule, overall rates significantly decreased as the dose of diazepam was increased.

The effects of diazepam on local rates of responding also depend on the ratio requirement (Fig. 1, right panel). Vehicle control rates were highest under the FR5 schedule and lowest under the FR20 schedule. Under the FR5 schedule, local rates first increased and then decreased as the dose of diazepam increased. Local rates were not systematically altered by diazepam under the FR10 schedule. Under the FR20 schedule, local rates of responding were significantly decreased as the dose of diazepam was increased.

Since some authors have argued that once a reinforcer is presented, subjects might adopt a "win-stay, lose-shift" strategy (e.g., [10,19]), it was of interest to examine responding within sessions where intermediate percentages of drug-

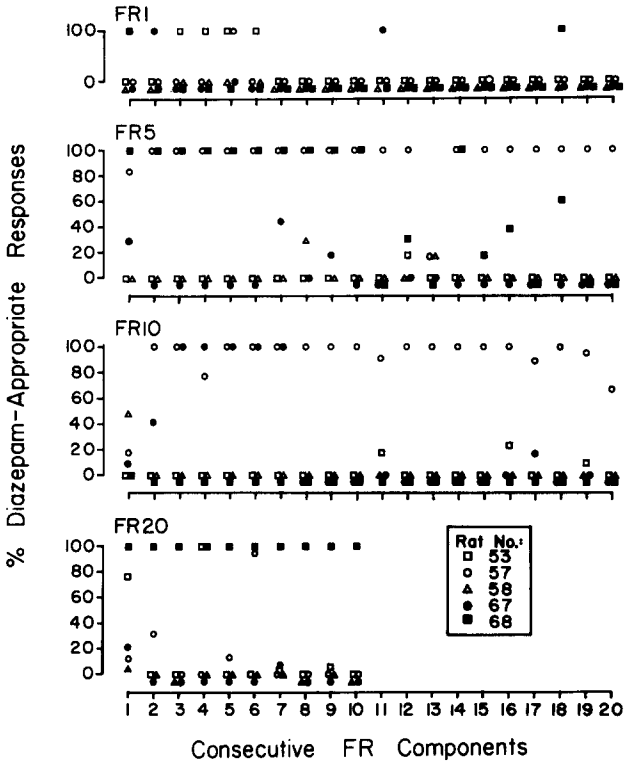

FIG. 2. Percentage of responses during each fixed-ratio component emitted on the diazepam-appropriate choice lever after the administration of 0.3 mg/kg of diazepam in individual rats trained to discriminate between saline and 1.0 mg/kg of diazepam under FR schedules of stimulus-shock termination. Abscissa: successive fixed-ratio components. Ordinates: percentage of the total responses during each FR component emitted on the diazepam-appropriate lever.

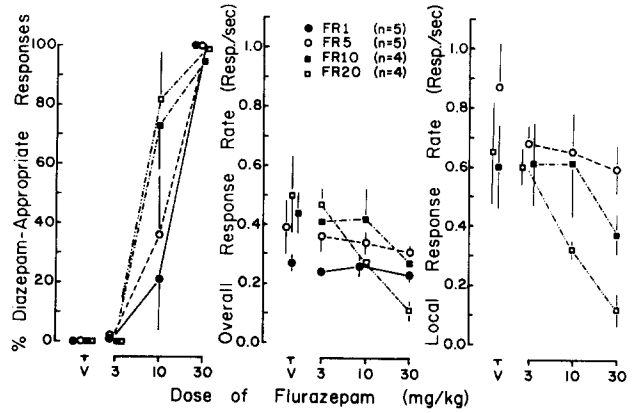

FIG. 3. Dose-effect curves for flurazepam in rats trained to discriminate between saline and 1.0 mg/kg of diazepam under fixed-ratio (FR) schedules of stimulus-shock termination. Each point is the mean of one observation in each of the rats (n=number of rats). Other details as in Fig. 1.

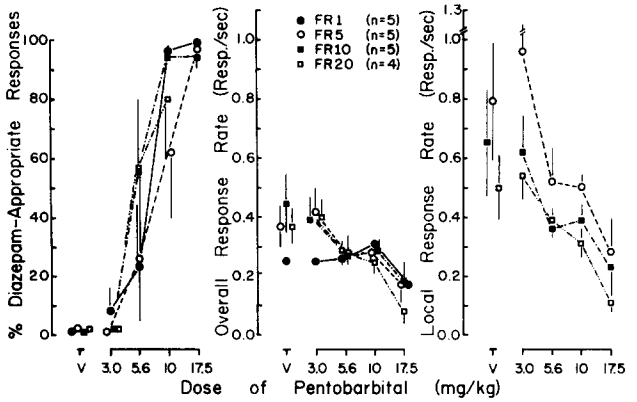

FIG. 4. Dose-effect curves for pentobarbital in rats trained to discriminate between saline and 1.0 mg/kg of diazepam under fixed-ratio (FR) schedules of stimulus-shock termination. Each point is the mean of one observation in each of the rats (n=number of rats). Other details as in Fig. 1.

appropriate responding occurred. Figure 2 presents the data for individual rats during each FR component during test sessions where 0.3 mg/kg of diazepam was administered before the test session. It may be seen in Fig. 2 that individual rats did not respond exclusively on one choice lever throughout the test sessions. For example, under the FR5 schedule, rat 68 responded only on the diazepam-appropriate lever during the first 10 FR components, but then switched and responded almost entirely on the saline-appropriate lever. Also, under the FR10 schedule, rat 67 responded primarily on the saline-appropriate lever during the first two components, on the diazepam-appropriate lever during the next five components, and then predominantly on the saline-appropriate lever for the remainder of the session. Similar results were obtained with intermediate doses of flurazepam and pentobarbital (data not presented). Thus, rats can and do distribute their responses on both choice levers during test sessions.

Flurazepam

Flurazepam (IP) also occasioned dose-related increases in diazepam-appropriate responding over the dose range of 3.0 to 30 mg/kg (Fig. 3, left panel). Vehicle and the lowest dose of flurazepam occasioned only responding on the saline-appropriate lever, whereas the highest dose of flurazepam occasioned greater than 95 percent diazepam-appropriate responding. The intermediate dose of flurazepam (10 mg/kg) occasioned intermediate percentages of responding on the diazepam-appropriate lever, the magnitude of which varied directly with the size of the FR value.

Rates of responding under all schedule values were either unchanged or decreased in a dose-related manner by flurazepam. Overall and local response rates (Fig. 3, middle and right panels, respectively) after the IP administration of flurazepam vehicle were similar in magnitude to rates observed after the SC administration of diazepam vehicle. Overall rates (Fig. 3, middle panel) were significantly decreased in a dose-related manner only under the FR20 schedule. Local response rates (Fig. 3, right panel) were significantly decreased by all doses under the FR5 schedule,

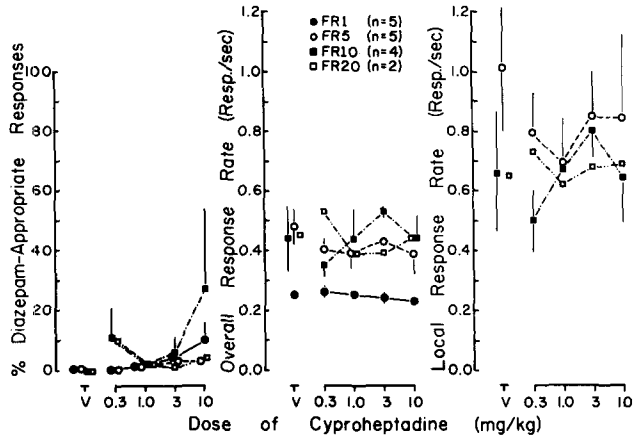

FIG. 5. Dose-effect curves for cyproheptadine in rats trained to discriminate between saline and 1.0 mg/kg of diazepam under fixed-ratio (FR schedules of stimulus-shock termination. Each point is the mean of one observation in each of the rats (n=number of rats). Other details as in Fig. 1.

by the 30 mg/kg dose under the FR10 schedule, and by the 10 and 30 mg/kg doses under the FR20 schedule.

Pentobarbital

Like diazepam and flurazepam, pentobarbital also occasioned dose-related increases in diazepam-appropriate responding (Fig. 4, left panel). Vehicle and the lowest dose of pentobarbital (3.0 mg/kg) occasioned less than 10 percent diazepam-appropriate responding. Doses of 5.6 and 10 mg/kg pentobarbital typically occasioned intermediate percentages of diazepam-appropriate responding, the magnitude of which varied with the FR value. A dose of 17.5 mg/kg of pentobarbital occasioned greater than 88 percent diazepam-appropriate responding under the FR1, FR5 and FR10 schedules. However, under the FR20 schedule, only one animal was able to respond after 17.5 mg/kg of pentobarbital; this animal emitted 79 percent diazepam-appropriate responses.

Overall and local response rates were only decreased in a dose-related manner by pentobarbital (Fig. 4, middle and right panels, respectively). Vehicle control rates were similar in magnitude to those observed with the diazepam vehicle. Under the three higher schedule values, both overall and local response rates significantly decreased as the dose of pentobarbital was increased from 3.0 to 17.5 mg/kg.

Cyproheptadine

Over the dose-ranges of 0.3 to 10 mg/kg, cyproheptadine occasioned only saline-appropriate responding (Fig. 5, left panel). Further, neither overall nor local response rates (Fig. 5, middle and right panels, respectively) were significantly altered by cyproheptadine.

DISCUSSION

Stimulus control by diazepam of behavior maintained under FR schedules of stimulus-shock termination was relatively unaffected by the magnitude of the response requirement. At all schedule parameters, there were no significant differences among dose-effect curves determined for diazepam, flurazepam, pentobarbital or cyproheptadine. However, there was a tendency at intermediate doses for intermediate percentages of diazepam-appropriate responding to be lower with the two lower ratio requirements and percentages to be higher with the two higher ratio requirements. Numerous studies have evaluated the stimulus control by drugs of behavior maintained under FR schedules of food or water presentation. Although the magnitude of the FR requirement has not been varied within a single study, previous findings compared across studies where behavior was maintained by food or water presentation are in general agreement with the present findings. For example, the pharmacologic properties of the discriminative effects of morphine were qualitatively similar in rats whose behavior was maintained under either an FR1 schedule of milk presentation (e.g., [14]) or an FR10 schedule of water presentation (e.g., [8,9]). Further, the present findings using FR schedules of stimulus-shock termination are virtually identical with previous findings in the rat using a discrete-trial procedure [23]. In fact, it has been a general finding that the discriminative stimulus properties of a large number of drug classes are relatively unaffected by the schedule of reinforcement under which behavior is maintained (see reviews in [17]).

In contrast, the effects of drugs on rates of responding are critically dependent upon the schedule of reinforcement and the consequent event maintaining the behavior (e.g., [18]). In the present study, the size of the ratio requirement determined the effects of the drugs on rates of responding. When the ratio requirement was one response, none of the drugs altered response rates. When the ratio requirement was five responses, diazepam (1.0 mg/kg) tended to increase response rates whereas flurazepam and pentobarbital decreased response rates. With ratio requirements of 10 and 20 responses, all three drugs had no significant effect or decreased response rates. Pentobarbital has been reported previously to decrease response rates in squirrel monkeys responding under an FR100 schedule of stimulus-shock termination [16]. In this same study, chlordiazepoxide also decreased rates of responding. The effects of diazepam and flurazepam on responding under FR schedules of stimulus-shock termination have not been previously reported. Diazepam and pentobarbital also generally decrease rates of responding maintained under FR schedules of food presentation [18,20]. On the other hand, rates of responding which have been suppressed by presentation of noxious stimuli are increased by benzodiazepines and barbiturates [5, 18, 20].

A theoretical concern in drug discrimination experiments has been whether the presentation of a reinforcer during generalization test sessions confounds the results (e.g., [6,10]). It has been argued, for example, that presentation of a reinforcer may lead subjects to adopt a "win-stay, lost-shift" stragety (e.g., [10,19]) and therefore only responses emitted during extinction or prior to the first presentation of a reinforcer should be used for measures of stimulus control. Several lines of evidence, however, argue against this viewpoint. First, extinction is a dynamic process that alters behavior. Most importantly, several studies have demonstrated that extinction increases the variability of response topography, including response location [1, 7, 13]. Thus, testing during extinction would be expected to provide spuriously low measures of stimulus control. Second, the presentation of a reinforcer does not necessarily lead to a "win-stay, lose-shift" strategy. Such an argument presupposes that behavior is more strongly under the control of stimuli associ-

ated with the schedule of reinforcement as compared to drug produced discriminative stimuli. However, numerous studies on stimulus control of behavior by drugs, including the present study, have reported that responding can and does occur on all choice levers within a test session, even after the presentation of a reinforcer (e.g., [21, 26, 27]; this report). Third, studies where time-courses of drug action have been determined within a single session have demonstrated that a subject can change from initially responding on the vehicle-appropriate lever to the drug-appropriate lever and back to the vehicle-appropriate lever [15, 21, 24]. And fourth, in studies using cumulative-dosing procedures to generate dose-effect curves within a single session, animals begin the session by responding on the vehicle-appropriate choice lever but may later switch, after sufficient doses of drug, and respond on the drug-appropriate choice lever even though they have been previously reinforced only for responding on the vehicle-appropriate lever [2,19]. Thus, the preponderance of data, including the present report, indicates that drug-produced discriminate stimuli, under appropriate circumstances, can control behavior more strongly than stimuli associated with the schedule of reinforcement.

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REFERENCES

1. Antonitis, J. J. Response variability in the white rat during conditioning, extinction and reconditioning. *J Exp Psychol* **42:** 273–281, 1951.
2. Bertalmio, A. J., S. Herling, R. Y. Hampton, G. Winger and J. H. Woods. A procedure for rapid evaluation of the discriminative stimulus effects of drugs. *J Pharmacol Methods* **7:** 289–299, 1982.
3. Brady, K. T. and R. L. Balster. Discriminative stimulus properties of phencyclidine and five analogues in the squirrel monkey. *Pharmacol Biochem Behav* **14:** 213–218, 1981.
4. Brady, K. T., R. L. Balster and E. L. May. Stereoisomers of N-allylnormetazocine: Phencyclidine-like behavioral effects on squirrel monkeys and rats. *Science* **215:** 178–180, 1982.
5. Cook, L. and J. Sepinwall. Relationship of anticonflict activity of benzodiazepines to brain receptor binding, serotonin, and GABA. *Psychopharmacol Bull* **16:** 30–32, 1980.
6. Colpaert, F. C., C. J. E. Niemegeers and P. A. J. Janssen. Theoretical and methodological considerations on drug discrimination learning. *Psychopharmacologia* **46:** 169–177, 1976.
7. Eckerman, D. A. and R. N. Lanson. Variability of response location for pigeons responding under continuous reinforcement, intermittent reinforcement, and extinction. *J Exp Anal Behav* **12:** 73–80, 1969.
8. Gianutsos, G. and H. Lal. Effect of loperamide, haloperidol and methadone in rats trained to discriminate morphine from saline. *Psychopharmacologia* **41:** 267–270, 1975.
9. Gianutsos, G. and H. Lal. Selective interaction of drugs with a discriminable stimulus associated with narcotic action. *Life Sci* **19:** 91–98, 1976.
10. Goudie, A. J. Discriminative stimulus properties of fenfluramine in an operant task: An analysis of its cue function. *Psychopharmacology (Berlin)* **53:** 97–102, 1976.
11. Haug, T. and K. G. Gotestam. The diazepam stimulus complex: Specificity in a rat model. *Eur J Pharmacol* **80:** 225–230, 1982.
12. Herling, S., E. H. Coale, R. J. Valentino, D. W. Hein and J. H. Woods. Narcotic discrimination in pigeons. *J Pharmacol Exp Ther* **214:** 139–146, 1980.
13. Herrnstein, R. J. Stereotypy and intermittent reinforcement. *Science* **133:** 2067–2069, 1961.
14. Hirschhorn, I. D. and J. A. Rosecrans. Generalization of morphine and lysergic acid diethylamide (LSD) stimulus properties to narcotic analgesics. *Psychopharmacology (Berlin)* **47:** 65–69, 1976.
15. Holtzman, S. G. Phencyclidine-like discriminative effects of opioids in the rat. *J Pharmacol Exp Ther* **214:** 614–619, 1980.
16. Katz, J. L. and J. E. Barrett. Ethanol, pentobarbital and chlordiazepoxide effects in squirrel monkeys responding under fixed-ratio food presentation and stimulus-shock termination schedules. *Psychopharmacology (Berlin)* **56:** 153–155, 1978.
17. Lal, H. (ed). *Discriminative Stimulus Properties of Drugs*. New York: Plenum Press, 1977.
18. McKearney, J. W. and J. E. Barrett. Schedule-controlled behavior and the effects of drugs. In: *Contemporary Research in Behavioral Pharmacology*, edited by D. E. Blackman and D. J. Sanger. New York: Plenum Press, 1978, pp. 1–68.
19. McMillan, D. E., D. A. Cole-Fullenwider, W. C. Hardwick and G. R. Wenger. Phencyclidine discrimination in the pigeon using color tracking under second-order schedules. *J Exp Anal Behav* **37:** 143–147, 1982.
20. Sanger, D. J. and D. E. Blackman. Rate-dependence and the effects of benzodiazepines. *Adv Behav Pharmacol* **3:** 1–20, 1981.
21. Shannon, H. E. Evaluation of phencyclidine analogs on the basis of their discriminative stimulus properties in the rat. *J Pharmacol Exp Ther* **216:** 543–551, 1981.
22. Shannon, H. E. Phencyclidine-like discriminative stimuli of (+) and (−)N-allylnormetazocine in rats. *Eur J Pharmacol* **84:** 225–228, 1982.
23. Shannon, H. E. and S. Herling. Discriminative stimulus effects of diazepam in rats: Evidence for a maximal effect. *J Pharmacol Exp Ther* **227:** 160–166, 1983.
24. Shannon, H. E., R. L. McQuinn, D. B. Vaupel and E. J. Cone. Effects of cycloalkylring analogs of phencyclidine on behavior in rodents. *J Pharmacol Exp Ther* **224:** 327–333, 1983.
25. Snedecor, G. W. and W. G. Cochran. *Statistical Methods*, 6th edition. Ames, IA: Iowa State University Press, 1967.
26. Stolerman, I. P. and G. D. D'Mello. Role of training conditions in discrimination of central nervous system stimulants by rats. *Psychopharmacology (Berlin)* **73:** 295–303, 1981.
27. White, J. M. and S. G. Holtzman. Three-choice drug discrimination in the rat: Morphine, cyclazocine and saline. *J Pharmacol Exp Ther* **217:** 254–262, 1981.