JOURNAL OF THE EXPERIMENTAL ANALYSIS OF BEHAVIOR 1986, 46, 363-379 NUMBER 3 (NOVEMBER)

A PHARMACOLOGICAL EXAMINATION OF THE RESISTANCE-TO-CHANGE HYPOTHESIS OF RESPONSE STRENGTH

STEVEN L. COHEN

BLOOMSBURG UNIVERSITY OF PENNSYLVANIA

The effects of *d*-amphetamine sulfate, sodium pentobarbital, haloperidol, and cholecystokinin-octapeptide were examined within the context of Nevin's (1974, 1979) resistance-to-change hypothesis of response strength. In three experiments, rats' responding was reinforced by delivery of food under chained random-interval 30-s random-interval 30-s, multiple fixed-interval 30-s fixed-interval 120-s, or multiple random-interval 30-s random-interval 120-s schedules. Each rat received several doses of each drug and changes in response rate were measured. The resistance-to-change hypothesis predicts greater disruption of response rate relative to baseline in the initial component of the chained schedule and in the 120-s component of the multiple schedules. In the chained schedule cholecystokinin-octapeptide produced greater reductions in response rate relative to baseline in the initial component. However, no differences between components were observed with haloperidol or sodium pentobarbital, and high doses of *d*-amphetamine reduced response rate in the terminal component relatively more than in the initial component. In the multiple schedules either no differences were observed between components or response rate was reduced more relative to baseline in the 30-s component. The data fail to support the notion that drugs may be viewed within the same context as other response disruptors such as extinction, satiation, and the presentation of alternative reinforcement.

Key words: resistance-to-change hypothesis, response strength, *d*-amphetamine, sodium pentobarbital, cholecystokinin-octapeptide, haloperidol, chained schedule, multiple schedule, lever press, rats

Nevin (1974, 1979) has argued that response strength may best be measured by the extent to which operant behavior resists change from disruptive sources. Variables such as rate, magnitude, and delay of reinforcement, traditionally thought to determine the strength of responding, have been shown to affect the degree of change produced by extinction, satiation, concurrent presentation of alternative reinforcement, conditioned suppression, and punishment. For example, when pigeons' responding was extinguished after being maintained under a multiple variable-interval (VI) 2-min VI 6-min schedule of reinforcement (Nevin, 1974), responding was reduced less relative to baseline in the component providing the greater rate of reinforcement. Greater resistance to change has also been observed in responses producing more immediate and greater magnitudes of reinforcement (Nevin, 1974). It has been shown that resistance to change is not determined by rate of response. Rate of reinforcement still determined the degree of response disruption when response rates were manipulated by the addition of differential-reinforcement-of-low and -high rate (DRL and DRH) contingencies (Nevin, 1974, 1979).

Studies examining the resistance-to-change hypothesis of response strength have typically used extinction, satiation, and alternative sources of reinforcement as response disruptors (Mandell, 1980; Nevin, 1974, 1979; Nevin, Mandell, & Atak, 1983; Nevin, Mandell, & Yarensky, 1981). Drugs may also be viewed in this context (see Branch, 1984). Pharmacological agents have been shown to disrupt operant baselines by increasing and decreasing response rates. Amphetamine, for example, has been shown to increase low response rates maintained by DRL and fixed-interval (FI) schedules of reinforcement (Clark & Steele, 1966; Heffner, Drawbaugh, & Zigmond, 1974; Lucki & DeLong, 1983; McMillan, 1979; McMillan & Healey, 1976;

Portions of this research were supported by a Faculty Release-Time Grant from Bloomsburg University of Pennsylvania. The author gratefully acknowledges the assistance of Mindy Crouse, Robin Drost, and Hank Reardin in conducting the research. Requests for reprints may be sent to Steven L. Cohen, Department of Psychology, Bloomsburg University of Pennsylvania, Bloomsburg, Pennsylvania 17815.

Zimmerman & Schuster, 1962) and to decrease or not affect high response rates maintained by variable-ratio, VI, and fixed-ratio schedules of reinforcement (Clark & Steele, 1966; Heffner et al., 1974; Lucki, 1983; Lucki & DeLong, 1983; Owen, 1960). These data have supported the rate-dependency hypothesis, which argues that control rate of response determines a drug's effect on response rate (e.g., Dews & Wenger, 1977).

The rate-dependency hypothesis has provided a framework for the analysis of a large body of pharmacological research. The present experiments were not designed to compare the resistance-to-change and rate-dependency hypotheses. Rather, they were an attempt to view changes in response rate following drugs in the context of the resistance-to-change hypothesis. If drugs act similarly to other response disruptors such as extinction, then greater drug-induced changes in response rate relative to baseline would be expected in components of multiple schedules with lower reinforcement rates or in the early components of chained schedules.

EXPERIMENT 1

Response strength in the initial component of a chained schedule would be expected to be lower than in the terminal component because of its relative time from reinforcement. Nevin et al. (1981) showed that responding in the initial component was less resistant to change from satiation and alternative reinforcement in a chained random-interval (RI) 40-s RI 40-s schedule. The present experiment examined the effects of *d*-amphetamine sulfate, sodium pentobarbital, haloperidol, and cholecystokinin-octapeptide (CCK8) on behavior controlled by a chained RI 30-s RI 30-s schedule. The drug CCK8 is an eight amino-acid peptide identified both in the brain and gastrointestinal tract (Beinfeld, Meyer, Eskay, Jensen, & Brownstein, 1981; Ivy & Oldberg, 1928) that depresses food intake in several species and is considered a putative mediator of short-term satiety signals (Maddison, 1977; Smith, 1984). It has also been shown to reduce exploration in the open field, social interactions, avoidance responding, and food- and water-reinforced operant responding (Cohen, Knight, Tamminga, & Chase, 1982, 1983, 1985; Maddison, 1977). Four different drugs were examined in this experiment in order to test the generality of the relationship between drugs and the resistance-to-change hypothesis. Although the four compounds have different pharmacological properties, they have all been shown to disrupt responding and therefore were predicted to produce greater changes in response rate in the initial component of the chained schedule.

METHOD

Subjects

Four male albino Sprague-Dawley rats (Camm Research) that weighed between 350 and 370 g prior to food deprivation were maintained at 80% of those free-feeding body weights. They had been used in a previous experiment 98 days earlier when they had received 15 sessions of RI 30-s training and a single injection of naloxone. They had free access to water and were kept on a 12:12 hr light/dark cycle with lights on at 0600.

Apparatus

A modular operant conditioning chamber for rats (Coulbourn Instruments) containing a food cup that protruded into the center of the work panel, a triple-cue lamp above the food cup, and a 28-V white houselight at the top center of the panel was housed in a sound-attenuating cubicle. The response lever was located on the right side of the work panel 28 mm from the grid floor and 22 mm from the right wall; it operated with a minimum force of approximately 0.24 N. A Gerbrands feeder delivered 45-mg Noyes food pellets. Contingencies were controlled by solid-state programming equipment (Coulbourn Instruments).

Drugs

d-Amphetamine sulfate (Sigma) and sodium pentobarbital (Sigma) were dissolved in physiological saline. CCK8 (Boeringer Mannheim) was dissolved in physiological saline with 1 M sodium bicarbonate added (50 μL/mL) to raise the pH to neutrality. Haloperidol (McNeil) came in liquid form (2 mg/mL) and was diluted with distilled water to the proper dose. For all experiments in this study, injections were given intraperitoneally in a volume of 1 mL/kg body weight. Injections of CCK8 were given 60 s before a ses-

sion and *d*-amphetamine, haloperidol, and sodium pentobarbital were given 20 min before a session.

Procedure

Training. Because they had received prior training, rats were placed directly on a RI 30-s schedule. In the presence of the steady houselight, the first lever press after an average of 30 s produced a food pellet, turned off the houselight, and turned on the yellow cue lamp above the feeder cup for 5 s. Responses during the 5-s feeder cycle had no scheduled consequences. Sessions were terminated after 60 reinforcements and were conducted Monday through Friday. After two sessions of RI 30-s, the rats were placed on a chained RI 10-s RI 10-s schedule. During the first component (the houselight flashing at a rate of two per second), the first response after an average of 10 s initiated the second component (steady houselight), in which the first response after an average of 10 s produced food. After the 5-s feeder cycle, the first component of the chain was reinstated. Rats were maintained on this schedule for one session, a chained RI 20-s RI 20-s schedule for one session and a chained RI 30-s RI 30-s schedule for the remainder of the experiment. Sessions were terminated after 40 reinforcements.

Drug treatment. Rats responded under the chained RI 30-s RI 30-s schedule for 38 sessions before response rate was considered to have stabilized (no increasing or decreasing response-rate trends in either component for at least five sessions) and the first injection was given. The first series of injections examined CCK8. Injections were given Tuesday and Friday of each week in the following sequence: 0 (saline plus sodium bicarbonate), 0.01, 0.1, 1, 10, 0, 5, 10, 0.1, 100 μg/kg. Next, *d*-amphetamine was given once each week in the following sequence: 0 (saline), 0.25, 0.5, 1, 0.25, 2, 0.125, 4 (Rat 38 only), 0, 1 mg/kg. A redetermination of the 2 mg/kg amphetamine injection was made after the second 16 mg/kg sodium pentobarbital injection (described below). Third, haloperidol injections were given once each week in the following sequence: 0 (water), 10, 100, 50, 75, 100 μg/kg. Rat 21 did not receive a second injection of 100 μg/kg. Last, sodium pentobarbital injections were given Tuesday and Friday of each week in the following sequence: 0 (saline), 0.5, 4, 8, 16, 12, 24, 32, 16, 8 mg/kg. During 25 days between the 24 and 32 mg/kg injections, no drugs were administered although sessions were conducted as usual. Rat 1 received only one 16 mg/kg sodium pentobarbital injection.

RESULTS

Average rate of responding was assessed for each component of the chained schedule by dividing total number of responses in a component by the time accrued in that component (not including feeder cycles). Responses and time prior to the first food presentation were excluded from analysis to account for bias that might have resulted from initial pausing in the first component where a response was required to produce the second component. Drug effects were expressed as the ratio of response rate during a drug session to baseline response rate ("proportion of baseline"), inasmuch as the resistance-to-change hypothesis predicts changes relative to baseline response rate. For each drug a baseline was calculated by averaging response rate in each nondrug session immediately preceding each drug session. (See Appendix for absolute response rates during baseline and drug sessions.) Where a second administration of a drug dose was made, the average ratio obtained in both determinations is presented in the figures.

As expected, baseline response rate under the chained schedule was considerably lower in the initial than in the terminal component (see Table A1, Appendix). In the CCK8 series, for example, baseline for the 4 rats in the initial component ranged from 11 to 27 responses per min compared to 71 to 150 in the terminal component. Figures 1 and 2 show changes in response rate relative to baseline following injections of the four compounds. Administration of CCK8 decreased responding in both components of the chained schedule at doses of approximately 1.0 μg/kg and higher. Decreases in response rate generally resulted from both a decrease in the number of responses and an increase in time spent in each component. Most importantly, responding decreased relatively more in the initial than in the terminal component for all 4 rats.

With administration of *d*-amphetamine, responding decreased at doses of 0.25 mg/kg and higher, although there were some exceptions (Component 1 for Rat 38 at 4 mg/kg

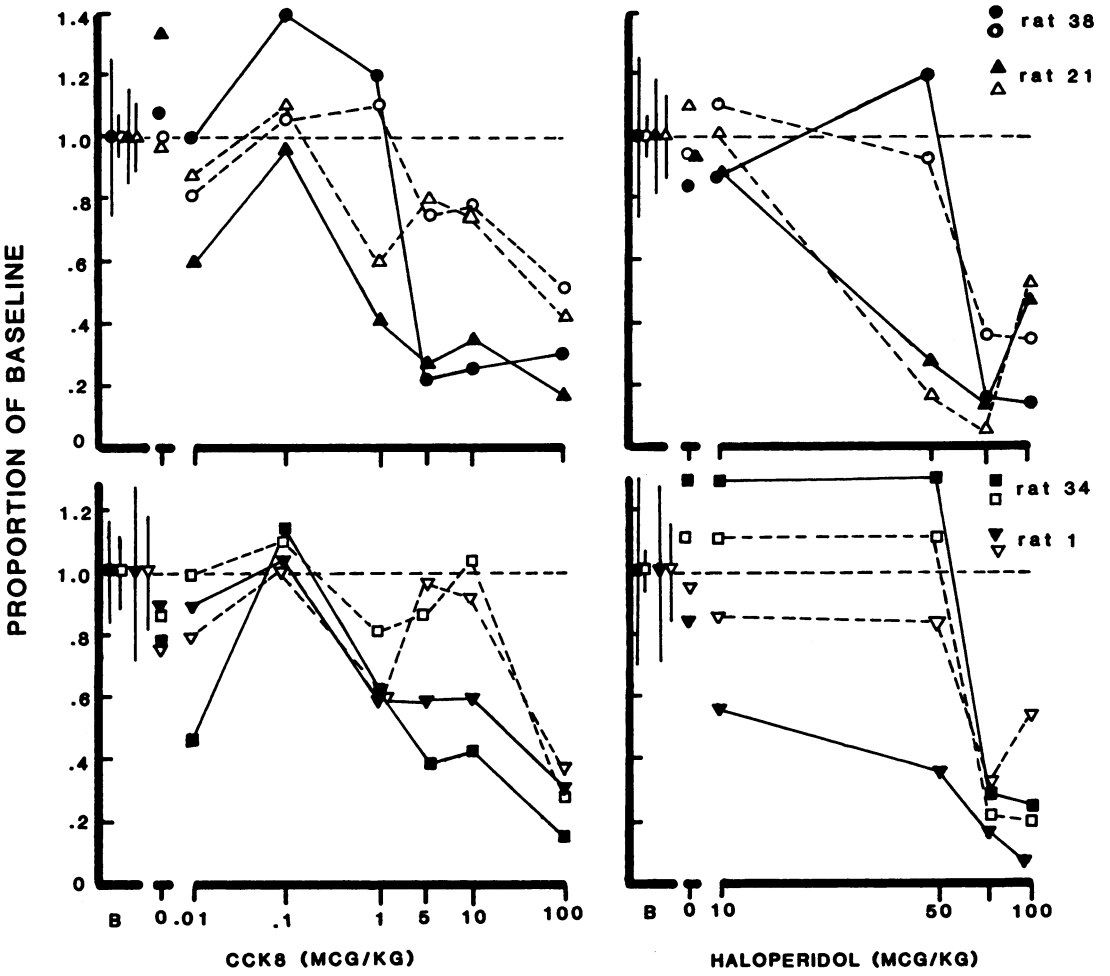

Fig. 1. The ratio of response rate during a drug session to baseline response rate ("proportion of baseline") in the initial RI 30-s (filled symbols) and terminal RI 30-s (open symbols) components of the chained schedule for CCK8 and haloperidol drug injections. Above B are the means and 95% confidence intervals for preinjection baseline sessions.

and Rat 1 at 1 and 2 mg/kg). At doses of 1 mg/kg and higher, responding decreased relatively more in the terminal component than in the initial component, although the difference was small for Rat 34. Examination of the absolute response rates (Table A1, Appendix) shows that response rate in the terminal component continued to decrease with increasing doses of *d*-amphetamine, whereas rate in the initial component was usually less affected. At the highest dose of *d*-amphetamine, the response rates of Rats 38 and 1 increased in the initial component of the chained schedule.

However, with the neuroleptic, haloperidol, responding decreased in both components of the chained schedule, and no consistent differences were observed between components. Sodium pentobarbital usually decreased response rate in both components at approximately 12 to 16 mg/kg and higher (Figure 2). Again, there were no consistent differences in relative changes in response rate between components. Rat 38 appeared to be unaffected by 32 mg/kg pentobarbital. However, this rat lay prone on the chamber floor during the first portion of the session, followed by recovery to normal baseline response rate.

Discussion

Nevin et al. (1981) observed greater response disruption in the initial component of a chained RI 40-s RI 40-s schedule following

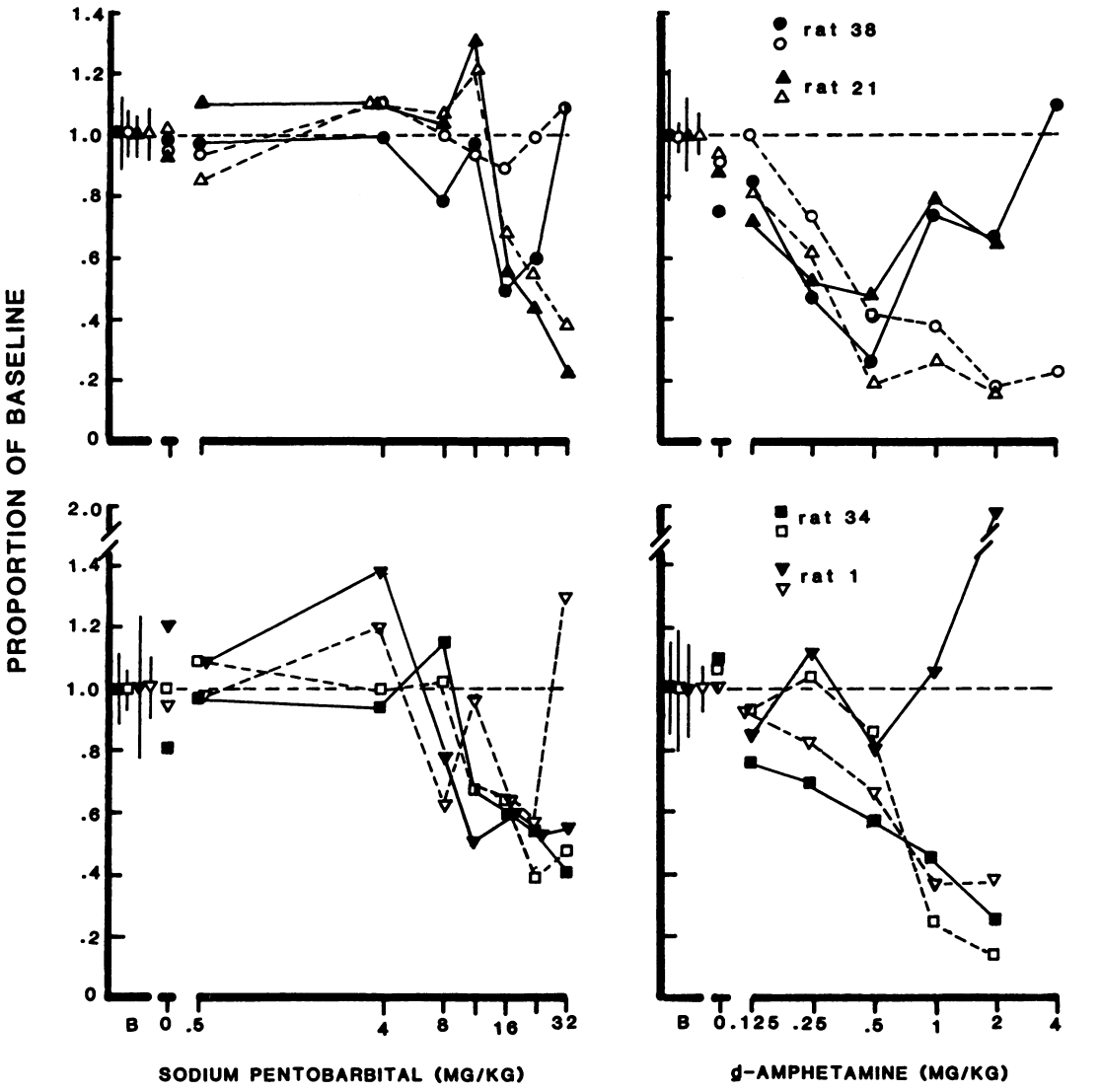

Fig. 2. The ratio of response rate during a drug session to baseline response rate ("proportion of baseline") in the initial RI 30-s (filled symbols) and terminal RI 30-s (open symbols) components of the chained schedule for sodium pentobarbital and *d*-amphetamine injections. Above B are the means and 95% confidence intervals for preinjection baseline sessions.

satiation and the presentation of alternative reinforcement. In the present study, greater response disruption was also observed in the initial component of a chained RI 30-s RI 30-s schedule following injections of CCK8. However, no consistent differences were found between initial and terminal components following haloperidol or sodium pentobarbital, and with *d*-amphetamine, high doses produced greater relative reductions in the terminal component than in the initial component. Experiment 2 further investigated the relationship between drugs and the resistance-to-change hypothesis by examining the effects of three drugs on a multiple FI 30-s FI 120-s schedule of reinforcement. According to the resistance-to-change hypothesis, greater disruption in baseline response rate was expected in the FI 120-s component. In addition to drug sessions, a nondrug extinction test was conducted to see if the present procedure would produce results similar to those reported in

traditional resistance-to-change experiments (e.g., Nevin, 1974).

EXPERIMENT 2

METHOD

Subjects and Apparatus

Three male albino Sprague-Dawley rats (Camm Research) were maintained at 80% of their free-feeding body weights. They weighed between 378 and 450 g prior to food deprivation, and had been used in a previous experiment 101 days earlier when they had received 20 sessions of RI 30-s training and a single injection of saline. The same experimental chamber used in Experiment 1 was used here except that the protruding food hopper was replaced with a recessed hopper and hopperlight, and the triple-cue lamp was removed.

Procedure

Training. Each rat was given one session of continuous reinforcement, two sessions under FI 20-s and two sessions under FI 60-s. Sessions ended after 60 reinforcements. Responding was then maintained on a multiple FI 30-s FI 120-s schedule for the rest of the experiment. In the first component of the multiple schedule (houselight flashing at a rate of two per second), the first response after 30 s from component onset produced food, turned off the houselight, and turned on the white hopperlight for 5 s. In the second component (steady houselight), the first response after 120 s produced food and the hopperlight. Responses during the 5-s food cycle had no scheduled effects. Components alternated following each food presentation. A 60-s limited hold was used with both fixed-interval schedules—that is, if no response occurred for 60 s after the fixed interval timed out, the component switched and food was not delivered. Each session began with the FI 30-s component and ended after a total of 40 components.

Drug treatment. The multiple FI 30-s FI 120-s schedule was in effect for 65 sessions before response rate was considered to have stabilized and the first injection was given. *d*-Amphetamine injections were given once each week in the following sequence of doses: 0 (saline), 0.25, 1, 0.5, 0.125, 2, 0, 2, 1 mg/kg. Rat 89 received only one injection of 2 mg/kg and failed to respond at this dose. Next, CCK8 was given once each week in the following sequence: 0 (saline plus sodium bicarbonate), 10, 1, 40, 10, 0 μg/kg. Rat 87 received additional injections of 200, 100, 150, 100 μg/kg, but did not receive a second saline or 10 μg/kg injection. Finally, sodium pentobarbital was given once each week in the following sequence: 0 (saline), 12, 24 mg/kg.

Extinction test. Three extinction sessions were conducted on consecutive days with no injections given. During these sessions, food and the 5-s feeder cycle were discontinued. The first component terminated automatically after 30 s and the second component after 120 s until 40 alternating components were completed.

RESULTS

Baseline response rate was lower in the FI 120-s than in the FI 30-s component (see Appendix, Table A2). For example, during the *d*-amphetamine injections, baseline response rate for the 3 rats in the FI 120-s component ranged from 14 to 19 responses per min compared to 26 to 30 responses per min in the FI 30-s component. Figure 3 shows changes in response rate relative to baseline following administration of the three compounds. There is no evidence that *d*-amphetamine disrupted response rates more in the FI 120-s than in the FI 30-s component. For Rat 66, an increasing dose of *d*-amphetamine produced a greater reduction in response rate relative to baseline in the FI 30-s than in the FI 120-s component. This effect was not consistently observed in Rats 89 and 87. There is no clear evidence that rates were consistently disrupted more in the FI 120-s component. Administration of CCK8 reduced response rate in both components. Again, there is no consistent evidence that CCK8 disrupted rates more in the FI 120-s than in the FI 30-s schedule. For Rat 66, response rates deviated more from baseline under the FI 30-s schedule. Rat 89 showed greater decreases in response rate in the FI 120-s component following 1 and 10 μg/kg but not 40 μg/kg. Rat 87, too, showed no consistent differences between components. Sodium pentobarbital decreased response rates in both components. With this drug, response rate consistently decreased more relative to baseline in the FI 30-s than in the FI 120-s component.

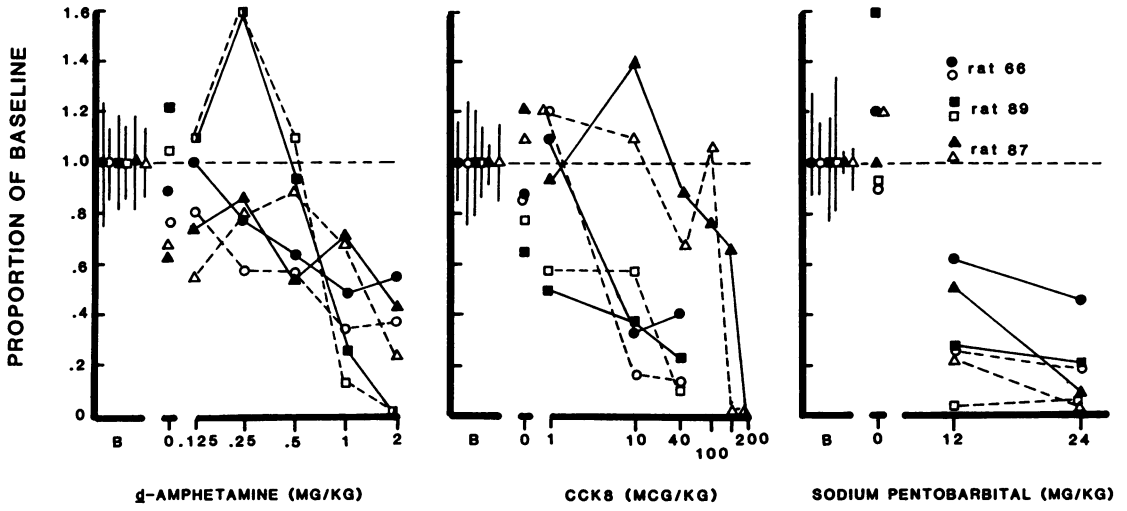

Fig. 3. The ratio of response rate during a drug session to baseline response rate ("proportion of baseline") in the FI 30-s (open symbols) and FI 120-s (filled symbols) components of the multiple schedule for *d*-amphetamine, CCK8, and sodium pentobarbital drug injections. Above B are the means and 95% confidence intervals for preinjection baseline sessions for *d*-amphetamine and CCK8. Ranges are presented under sodium pentobarbital instead of confidence intervals because confidence intervals were not appropriate with only three baseline data points.

Response rate is one aspect of behavior disrupted by drugs; response patterning under fixed-interval schedules is also susceptible to disruption (Branch & Gollub, 1974). If behavior has greater response strength in the FI 30-s component, as predicted by the resistance-to-change hypothesis, then drugs should have less effect on the typical positively accelerated pattern of responding in this component than in the FI 120-s component. To examine this, cumulative responses in successive sixths of the FI 30-s and FI 120-s schedules were recorded and an index of curvature was computed. The index (Fry, Kelleher, & Cook, 1960) is a statistic that measures the degree of patterning in fixed-interval schedules. A value of 0 indicates a constant response rate across segments of the fixed interval, and higher values indicate greater curvature, reaching 0.83 when the fixed interval is divided into sixths and all responding is limited to the last segment. Table 1 shows index of curvature under baseline and drug conditions. Only data from sessions following *d*-amphetamine injections are presented because with this drug a substantial amount of responding was maintained across the entire dose range. If response rates become too low, the index becomes an unreliable measure of patterning. Clearly, substantial response patterning occurred within both fixed-interval schedules. For 2 of the 3 rats, the degree of positively accelerated responding was almost identical in both components. *d*-Amphetamine lowered index of curvature, indicating a more constant response rate across segments of the fixed intervals. Figure 4 shows the ratio of the index obtained during drug sessions to the baseline index. The disruption to response patterning was similar in both components.

Figure 5 shows the results of the extinction test. For all rats, response rate in the FI 120-s component was consistently reduced more relative to baseline than was responding in the FI 30-s component.

Discussion

The results of the traditional extinction test support the resistance-to-change hypothesis, showing that the component providing the greater rate of reinforcement (i.e., FI 30-s) was more resistant to the disruptive effects of extinction. This finding indicates that the present procedure could produce results consistent with previous literature (e.g., Nevin, 1974). The effects of the drugs, however, did not support the resistance-to-change hypothesis. On the contrary, it appears that sodium pentobarbital produced greater relative disruptions of response rate in the FI 30-s than in the FI 120-s component. No consistent difference was observed following CCK8 or

Table 1

Index of Curvature for Component 1 (FI 30-s) and Component 2 (FI 120-s) of the multiple schedule during sessions following administration of *d*-amphetamine. Baseline (mean) and 95% confidence intervals are for preinjection sessions.

Component	Rat 87		Rat 89		Rat 66	
	1	2	1	2	1	2
	d-Amphetamine sulfate (mg/kg)					
Baseline	.60	.61	.61	.60	.43	.52
Conf. int.	.62–.58	.63–.59	.63–.59	.65–.55	.45–.41	.57–.47
Drug dose						
0	.55	.54	.49	.51	.43	.50
0	.61	.60	.62	.64	.44	.53
0.125	.64	.59	.64	.57	.49	.56
0.25	.52	.46	.52	.49	.45	.54
0.5	.55	.55	.52	.54	.40	.40
1	.51	.31	.29	.19	.24	.29
1	.24	.26	.14	.18	.42	.39
2	.20	.08	—	—	.05	.00
2	.02	.05	—	—	.23	.30

d-amphetamine. Fixed-interval response patterning was not differentially disrupted either (Figure 4). In light of these findings, a third experiment was conducted to explore further the relationship between the resistance-to-change hypothesis and drug effects. Rats were trained under a multiple RI 30-s RI 120-s schedule of reinforcement and given CCK8, *d*-amphetamine, and sodium pentobarbital. Again, according to the resistance-to-change hypothesis, greater disruption in response rate in the RI 120-s component was predicted.

EXPERIMENT 3

METHOD

Subjects and Apparatus

Four male albino Sprague-Dawley rats (Camm Research) were maintained at 80% of their free-feeding body weights, which ranged from 325 to 400 g. They had previous training under a fixed-ratio schedule of reinforcement but were drug naive. Four experimental chambers identical to the one described in Experiment 2 were controlled by an IBM-PC computer, Coulbourn Lab-Linc® interface, and Pascal programming. Each rat was assigned to one chamber.

Procedure

Training. The rats were exposed to a multiple RI 30-s RI 30-s schedule for two sessions, a multiple RI 30-s RI 60-s schedule for three sessions, and then a multiple RI 30-s RI 120-s schedule for the rest of the experiment. In the first component of the multiple schedule (houselight flashing at a rate of two per second), the first response after an average interval of 30 s produced food, turned on the hopperlight, and turned off the houselight for 5 s. In the second component (steady houselight), the first response after an average of 120 s produced food. Components alternated throughout the session with each component lasting 90 s. Each session began with Component 1 and terminated after 40 components.

Drug treatment. The multiple RI 30-s RI 120-s schedule was run for 46 sessions before response rate was considered to have stabilized and the first injection was given. Injections were spaced from 3 to 7 days apart. The first injections were CCK8 given in the following sequence of doses: 0 (saline plus sodium bicarbonate), 1, 5, 20, 40 μg/kg. The second injections were sodium pentobarbital given in the following sequence: 0 (saline), 16, 24, 12 mg/kg. The last injections were *d*-amphetamine given in the following sequence: 0 (saline), 1, 2, 0.5, 0.25, 0.125 mg/kg. Additional *d*-amphetamine injections of 0.5, 1, 2, 4, 8, 12 mg/kg were given to different rats in an irregular sequence.

Extinction test. Three extinction sessions were conducted with no injections; during these sessions, food and the 5-s feeder cycle

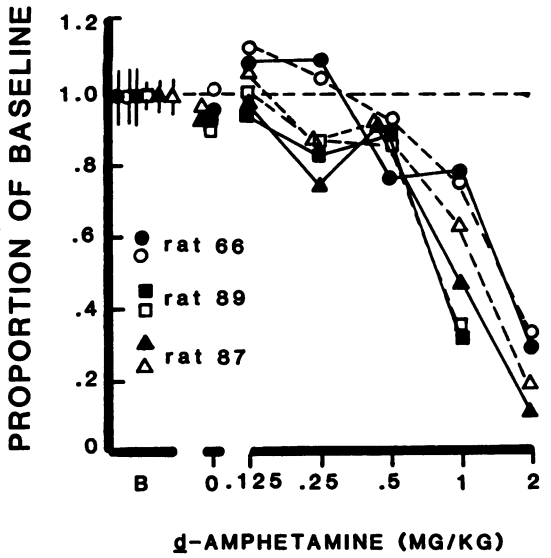

Fig. 4. The ratio of Index of Curvature during sessions following administration of *d*-amphetamine, to corresponding baseline sessions. Larger values of the index indicate greater acceleration of responding within the fixed-interval schedule. Data from the FI 30-s schedule are represented by open symbols, and data from the FI 120-s components of the multiple schedule are represented by filled symbols. Above B are the means and 95% confidence intervals for preinjection baseline sessions.

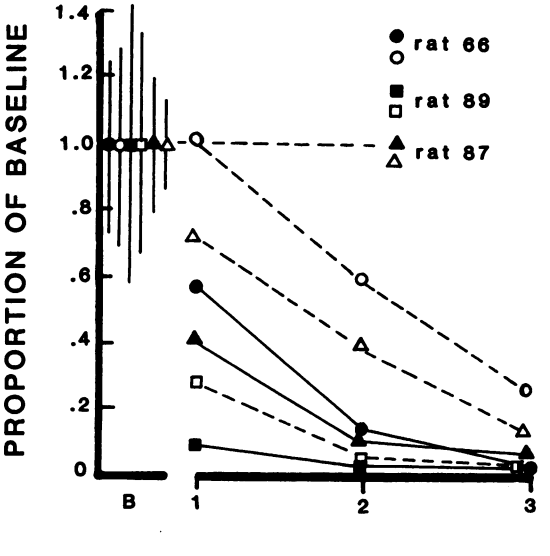

Fig. 5. The ratio of response rate during an extinction session to baseline response rate ("proportion of baseline") during three consecutive extinction sessions in the FI 30-s (open symbols) and FI 120-s (filled symbols) components of the multiple schedule. Above B are the means and 95% confidence intervals for preinjection baseline sessions.

were discontinued. Each component terminated automatically after 90 s and a session was comprised of 40 components.

Results

Baseline response rate was considerably higher in the RI 30-s than in the RI 120-s component. For example, in the baseline sessions preceding administrations of CCK8, response rate for the 4 rats ranged from 35 to 61 responses per min under the RI 120-s schedule and from 89 to 120 responses per min under the RI 30-s schedule (see Appendix, Table A3). Figure 6 shows the effects of the three drugs on baseline response rate. Injection of CCK8 reduced response rate in all rats. No consistent differences were observed between responding in the two components. Injection of sodium pentobarbital decreased response rate in both components. At high doses (16 and 24 mg/kg for Rats 82 and 98; 24 mg/kg for Rats 81 and 99), response rate decreased more relative to baseline in the RI 30-s component. Injections of *d*-amphetamine decreased response rate in both components. In the higher dose range (e.g., 1 to 4 mg/kg, Rat 82) response rates tended to decrease more relative to baseline in the RI 30-s component than in the RI 120-s components.

Figure 7 presents the effects of extinction on response rate. During the extinction sessions, response rate consistently decreased more relative to baseline in the RI 120-s than in the RI 30-s component, although the difference was very small for Rat 99.

Discussion

Nevin (1974) exposed pigeons to a multiple VI 2-min VI 6-min schedule of reinforcement, and then to extinction. As the resistance-to-change hypothesis predicts, responding was more resistant to extinction during the VI 2-min component. The results of the present extinction test confirm this finding. Rats' responding was more resistant to change in the RI 30-s than in the RI 120-s component. However, the data from the drug sessions do not support the resistance-to-change hypothesis. No consistent differences in response-rate reduction were observed between components after CCK8 injections, and there was a tendency following high doses of *d*-amphetamine and sodium pentobarbital for greater re-

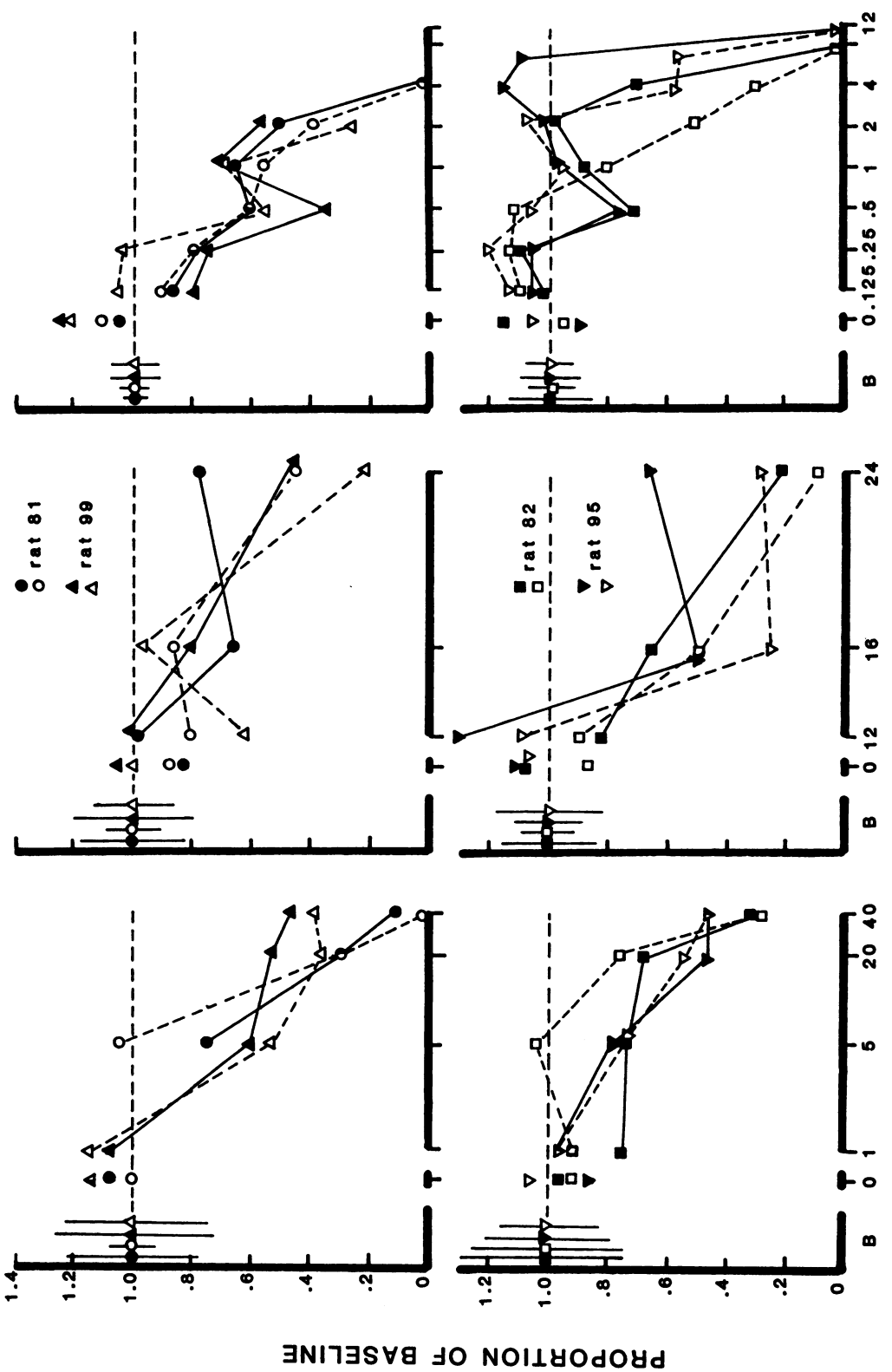

Fig. 6. The ratio of response rate during a drug session to baseline response rate ("proportion of baseline") in the RI 30-s (open symbols) and RI 120-s (filled symbols) components of the multiple schedule for sessions following injections of CCK8, sodium pentobarbital, and *d*-amphetamine. Above B are the means and 95% confidence intervals for preinjection baseline sessions.

sponse disruption to occur in the component providing the greater rate of reinforcement (RI 30-s).

GENERAL DISCUSSION

It has been shown that rate of reinforcement determines the extent of change in response rate produced by the disruptive sources of extinction, satiation, and the presentation of alternative reinforcement. In multiple VI VI schedules (Nevin, 1974; Nevin et al., 1983) and chained RI RI schedules (Nevin et al., 1981), response rate in a component with a higher reinforcement rate was less disrupted relative to baseline than was response rate in a component signaling a lower reinforcement rate. Similar results were obtained in the present study when responding was extinguished under multiple FI 30-s FI 120-s and multiple RI 30-s RI 120-s schedules: Response rate was reduced more relative to baseline in the 120-s than in the 30-s components.

Results from the pharmacological manipulations in the present studies do not support the notion that drugs may be viewed in the same context as other response disruptors. In most cases, injections of the drugs decreased response rate. Under the chained schedule, the resistance-to-change hypothesis was supported by data from the CCK8 injections: Response rate was reduced more relative to baseline in the initial component of the chained schedule. However, no differences between components were observed with haloperidol or sodium pentobarbital; with *d*-amphetamine, high doses produced more disruption in the terminal component. Under the two multiple schedules, either no consistent differences were observed between components or greater disruption occurred in the 30-s component.

The resistance-to-change hypothesis emphasizes reinforcement parameters as prime determiners of response change. In the present study, reinforcement rate was not a consistent predictor of relative changes in response rate. These data are consistent with those of Lucki and DeLong (1983) who exposed rats to a multiple random-ratio (RR) 20 RR 50 schedule of reinforcement. This schedule produced similar response rates but with different reinforcement rates. Although the resistance-to-change hypothesis predicts greater disruption

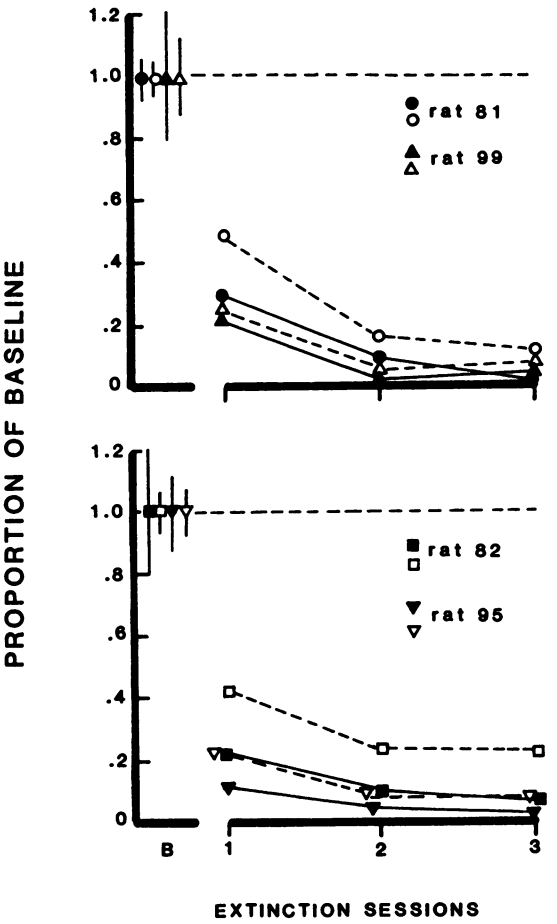

Fig. 7. The ratio of response rate during an extinction session to baseline response rate ("proportion of baseline") during three consecutive extinction sessions in the RI 30-s (open symbols) and RI 120-s (filled symbols) components of the multiple schedule. Above B are the means and 95% confidence intervals for preinjection baseline sessions.

in the RR 50 component because of its lower reinforcement rate, *d*-amphetamine decreased response rates equally in both components. Because baseline response rates were almost identical, it is possible that in Lucki and DeLong's study the rats did not show differential effects in both components following *d*-amphetamine because they failed to discriminate between the two random-ratio components. In the present study, however, stimulus control was clearly demonstrated by consistent differences in baseline response rates corresponding to components of higher and lower rates of reinforcement. Similarly, Rees,

Wood, and Laties (1985) exposed rats to a multiple schedule in which each component required a fixed number of responses on one lever before a response on a second lever was reinforced (i.e., fixed-consecutive-number schedule of reinforcement). In one component, a stimulus signaled when a switch to the second lever could be reinforced, but no signal occurred in the other component. Both components were arranged to provide the same rate of reinforcement, yet *d*-amphetamine disrupted switching performance more in the unsignaled component. The authors argued that rate of reinforcement plays only a minimal role in determining a drug's effect on response disruption, except perhaps as a determiner of response rate. Instead, they emphasized the importance of stimulus control as a factor in determining drug effects.

Nevin (1979) has related the resistance-to-change hypothesis to Herrnstein's (1970, 1974) formula for describing changes in response rate as a function of reinforcement rate. Recently, other investigators (Bradshaw, Ruddle, & Szabadi, 1981; Heyman, 1983; Heyman & Seiden, 1985) have applied Herrnstein's formula to study the effects of drugs on response rates. According to the formula, $P = kR/(R + R_o)$, P represents response rate, R represents reinforcement rate, and k and R_o are constants derived from the data that represent the maximum response rate that can be obtained in the experimental situation and the rate of alternative sources of reinforcement, respectively. Heyman (Heyman, 1983; Heyman & Seiden, 1985) has proposed that in pharmacology experiments, k reflects drug-induced alterations in response topography such as a motor deficit, an increase in pausing, or stereotypy. R_o is thought to reflect changes in reinforcement efficacy (i.e., quality or hedonic properties of the reinforcer). It has been shown that drugs may independently affect these two parameters (Heyman & Seiden, 1985).

As noted previously (Nevin, 1979), the resistance-to-change formulation is not incompatible with Herrnstein's (1970, 1974) formulation in situations where R_o varies and k remains unchanged. With k held constant, changes in R_o will produce larger deviations from baseline response rate (P) when reinforcement rate (R) is low than when it is high. However, the two formulations are not compatible in cases where k varies and R_o remains unchanged. In this situation changes in response rate are independent of baseline reinforcement rate. According to Herrnstein's formulation, the magnitude of drug-induced disruptions in baseline response rate should vary inversely with reinforcement rate only in situations where the drug affects reinforcement efficacy (R_o) and not when it simply affects response topography (k). In order to examine this formulation, Heyman's (1983) data were reanalyzed in terms of the resistance-to-change hypothesis. Heyman established stable responding in rats under a five-component multiple schedule that ranged from VI 10-s to VI 160-s; he then administered *d*-amphetamine and the neuroleptic, pimozide. Injections of *d*-amphetamine increased response rate at low doses and decreased rate at high doses. These changes in response rate were accompanied by changes in reinforcement efficacy (R_o) but not by systematic changes in response topography (k). When the data were reexamined by taking the ratio of drug response rate to baseline response rate, greater deviations from baseline were observed in components with lower reinforcement rates—a finding that is consistent with both Herrnstein's and Nevin's formulations. These data are not consistent, however, with those of the present study where *d*-amphetamine did not differentially affect response disruption in RI components of high and low reinforcement rate. Several differences between Heyman's (1983) study and the present study could have accounted for the different findings. Heyman, for example, used liquid reinforcers, longer component durations, a wider range of reinforcement rates across components, and had much lower response rates in the low reinforcement-rate components.

Unlike *d*-amphetamine, pimozide in Heyman's (1983) study produced a decrease in response rate that was accompanied by an increase in R_o and a decrease in k. Heyman showed that the ratio of drug response rate to baseline rate under pimozide did not consistently change as a function of the VI schedule. Similarly, Bradshaw et al. (1981) delivered *d*-amphetamine to rats responding under various VI schedules of reinforcement (they did not use multiple schedules). In this case, changes in response rate following administration of *d*-amphetamine were accompanied

by changes in both R_0 and k. A reanalysis of their data in terms of the ratio of drug response rate to control response rate did not show a strong relationship between the size of the ratio and the value of the VI schedule except at the two extreme VI values. Thus, the resistance-to-change hypothesis accommodated the data when the drugs produced changes in reinforcement efficacy (R_0), but not when they also produced changes in response topography (k). Perhaps one reason why the present data failed to show strong support for the resistance-to-change hypothesis was that drugs produced significant changes in response topography.

Historically, measures of response strength have included latency and magnitude of response, probability of response, resistance to extinction, and response rate (e.g., Nevin, 1979). These measures of behavior have provided orderly relationships between responding and operations thought to affect response strength, such as reinforcer presentation and extinction. The resistance-to-change hypothesis has attempted to account for response strength in terms of relative changes in response rate following exposure to disruptive sources. As initially presented, the resistance-to-change model does not place limitations on the nature of the disruptive source. In fact, the model has accounted well for effects of many sources of disruption such as extinction, satiation, concurrent presentation of alternative reinforcement, conditioned suppression, and punishment. Although the drugs used in the present study may have had differing and unrelated sensory, motivational, and motoric effects on the organism, they were all disruptive sources; yet the model failed to account for the relative changes in response rate following drug administration. These data do not suggest that the concept of response strength cannot be related to drug effects. The data do, however, establish limitations for the resistance-to-change hypothesis of response strength.

REFERENCES

Beinfeld, M. C., Meyer, D. K., Eskay, R. L., Jensen, R. T., & Brownstein, M. J. (1981). The distribution of cholecystokinin immunoreactivity in the central nervous system of the rat as determined by radioimmunoassay. *Brain Research,* **212,** 51–57.

Bradshaw, C. M., Ruddle, H. V., & Szabadi, E. (1981). Relationship between response rate and reinforcement frequency in variable-interval schedules: III. The effect of *d*-amphetamine. *Journal of the Experimental Analysis of Behavior,* **36,** 29–39.

Branch, M. N. (1984). Rate dependency, behavioral mechanisms, and behavioral pharmacology. *Journal of the Experimental Analysis of Behavior,* **42,** 511–522.

Branch, M. N., & Gollub, L. R. (1974). A detailed analysis of the effects of *d*-amphetamine on behavior under fixed-interval schedules. *Journal of the Experimental Analysis of Behavior,* **21,** 519–539.

Clark, F. C., & Steele, B. J. (1966). Effects of *d*-amphetamine on performance under a multiple schedule in the rat. *Psychopharmacologia,* **9,** 157–169.

Cohen, S. L., Knight, M., Tamminga, C. A., & Chase, T. N. (1982). Cholecystokinin-octapeptide effects on conditioned-avoidance behavior, stereotypy and catalepsy. *European Journal of Pharmacology,* **83,** 213–222.

Cohen, S. L., Knight, M., Tamminga, C. A., & Chase, T. N. (1983). Minimized tolerance to the suppressive effects of CCK8 on operant responding. *Behavioral and Neural Biology,* **39,** 123–127.

Cohen, S. L., Knight, M., Tamminga, C. A., & Chase, T. N. (1985). A comparison of peripheral and central effects of CCK8 on water-reinforced operant responding. *European Journal of Pharmacology,* **116,** 229–238.

Dews, P. B., & Wenger, G. R. (1977). Rate-dependency of the behavioral effects of amphetamine. In T. Thompson & P. B. Dews (Eds.), *Advances in behavioral pharmacology* (Vol. 1, pp. 167–227). New York: Academic Press.

Fry, W., Kelleher, R. T., & Cook, L. (1960). A mathematical index of performance on fixed-interval schedules of reinforcement. *Journal of the Experimental Analysis of Behavior,* **3,** 193–199.

Heffner, T. G., Drawbaugh, R. B., & Zigmond, M. J. (1974). Amphetamine and operant behavior in rats: Relationship between drug effect and control response rate. *Journal of Comparative and Physiological Psychology,* **86,** 1031–1043.

Herrnstein, R. J. (1970). On the law of effect. *Journal of the Experimental Analysis of Behavior,* **13,** 243–266.

Herrnstein, R. J. (1974). Formal properties of the matching law. *Journal of the Experimental Analysis of Behavior,* **21,** 159–164.

Heyman, G. M. (1983). A parametric evaluation of the hedonic and motoric effects of drugs: Pimozide and amphetamine. *Journal of the Experimental Analysis of Behavior,* **40,** 113–122.

Heyman, G. M., & Seiden, L. S. (1985). A parametric description of amphetamine's effect on response rate: Changes in reinforcement efficacy and response topography. *Psychopharmacology,* **85,** 154–161.

Ivy, A. C., & Oldberg, E. (1928). A hormone mechanism for gall bladder contraction and evacuation. *American Journal of Physiology,* **85,** 381–383. [Abstract]

Lucki, I. (1983). Rate-dependent effects of amphetamine on responding under random-interval schedules of reinforcement in the rat. *Pharmacology Biochemistry and Behavior,* **18,** 195–201.

Lucki, I., & DeLong, R. E. (1983). Control rate of response or reinforcement and amphetamine's effect on behavior. *Journal of the Experimental Analysis of Behavior,* **40,** 123–132.

Maddison, S. (1977). Intraperitoneal and intracranial cholecystokinin depress operant responding for food. *Physiology & Behavior,* **19,** 819–824.

Mandell, C. (1980). Response strength in multiple periodic and aperiodic schedules. *Journal of the Experimental Analysis of Behavior,* **33,** 221–241.

McMillan, D. E. (1979). Effects of *d*-amphetamine and caffeine on schedule-controlled and schedule-induced responding. *Journal of the Experimental Analysis of Behavior,* **32,** 445–456.

McMillan, D. E., & Healey, M. L. (1976). Some effects of *d*-amphetamine and pentobarbital on performance under a long fixed-interval schedule. *Journal of the Experimental Analysis of Behavior,* **25,** 389–399.

Nevin, J. A. (1974). Response strength in multiple schedules. *Journal of the Experimental Analysis of Behavior,* **21,** 389–408.

Nevin, J. A. (1979). Reinforcement schedules and response strength. In M. D. Zeiler & P. Harzem (Eds.), *Advances in analysis of behaviour: Vol. 1. Reinforcement and the organization of behaviour* (pp. 117–158). Chichester, England: Wiley.

Nevin, J. A., Mandell, C., & Atak, J. R. (1983). The analysis of behavioral momentum. *Journal of the Experimental Analysis of Behavior,* **39,** 49–59.

Nevin, J. A., Mandell, C., & Yarensky, P. (1981). Response rate and resistance to change in chained schedules. *Journal of Experimental Psychology: Animal Behavior Processes,* **7,** 278–294.

Owen, J. E., Jr. (1960). The influence of *dl, d-*, and *l*-amphetamine and *d*-methamphetamine on a fixed-ratio schedule. *Journal of the Experimental Analysis of Behavior,* **3,** 293–310.

Rees, D. C., Wood, R. W., & Laties, V. G. (1985). The roles of stimulus control and reinforcement frequency in modulating the behavioral effects of *d*-amphetamine in the rat. *Journal of the Experimental Analysis of Behavior,* **43,** 243–255.

Smith, G. P. (1984). Gut hormone hypothesis of postprandial satiety. In A. J. Stunkard & E. Stellar (Eds.), *Psychobiology of eating and its disorders* (pp. 67–75). New York: Raven Press.

Zimmerman, J., & Schuster, C. R. (1962). Spaced responding in multiple DRL schedules. *Journal of the Experimental Analysis of Behavior,* **5,** 497–504.

Received August 30, 1985
Final acceptance August 11, 1986

APPENDIX

Table A1

Summary of absolute response rate (responses per min) during sessions following administrations of CCK8, *d*-amphetamine sulfate, haloperidol, and sodium pentobarbital for Component 1 (initial RI 30-s) and Component 2 (terminal RI 30-s) of the chained schedule. Baseline (mean) and 95% confidence intervals are based upon preinjection sessions. Note that the confidence intervals do not always bracket the mean equally, because of rounding error.

Component	Rat 38		Rat 34		Rat 21		Rat 1	
	1	2	1	2	1	2	1	2
				CCK8 (μg/kg)				
Baseline	17	87	27	150	24	127	11	71
Conf. int.	21–13	94–81	32–23	168–133	28–19	143–112	14–8	84–59
Drug dose								
0	24	96	12	92	33	124	12	46
0	13	79	29	161	30	125	8	61
0.01	18	71	13	156	14	111	10	56
0.1	31	88	33	165	17	130	11	59
0.1	17	92	29	169	29	155	12	86
1	20	92	17	122	9	75	7	43
5	4	65	11	130	6	102	7	69
10	4	57	9	147	5	54	10	60
10	4	78	14	164	8	94	4	69
100	5	45	4	43	4	52	4	27

APPENDIX

Table A1 (*continued*)

Component	Rat 38		Rat 34		Rat 21		Rat 1	
	1	2	1	2	1	2	1	2
				d-Amphetamine sulfate (mg/kg)				
Baseline	17	99	20	121	26	114	8	63
Conf. int.	20–13	102–95	23–18	145–97	29–22	121–107	9–7	68–58
Drug dose								
0	15	87	22	111	23	99	7	58
0	11	95	22	141	22	115	9	70
0.125	14	100	15	112	18	92	7	59
0.25	4	65	11	118	11	62	10	58
0.25	12	81	17	130	15	79	7	45
0.5	4	40	12	104	12	23	6	42
1	13	46	15	56	21	34	12	30
1	13	29	3	8	19	26	5	19
2	17	25	7	19	17	22	17	28
2	5	9	4	15	16	21	14	22
4	19	23	—	—	—	—	—	—
				Haloperidol (μg/kg)				
Baseline	20	103	24	122	22	104	8	71
Conf. int.	25–15	111–96	32–16	131–114	26–18	118–90	11–6	83–60
Drug dose								
0	17	98	31	138	21	110	7	68
10	17	109	30	132	19	104	5	60
50	24	96	32	133	6	18	3	60
75	3	38	7	26	3	6	1	23
100	2	57	8	21	2	8	1	27
100	4	15	4	27	—	—	1	50
				Sodium pentobarbital (mg/kg)				
Baseline	20	101	25	108	20	95	7	64
Conf. int.	23–18	108–94	28–22	115–100	21–19	104–87	8–5	71–58
Drug dose								
0	20	96	20	109	18	95	8	61
0.5	20	95	24	116	21	80	8	63
4	21	107	23	112	23	105	9	78
8	18	107	31	114	14	92	1	23
8	14	90	23	99	27	113	10	56
12	20	97	17	72	25	110	4	63
16	8	82	14	68	8	37	—	—
16	12	98	15	66	14	98	4	42
24	12	102	13	43	9	50	4	38
32	22	107	10	51	5	37	4	86

APPENDIX

Table A2

Summary of absolute response rate (responses per min) during sessions following administrations of *d*-amphetamine, CCK8, and sodium pentobarbital for Component 1 (FI 30-s) and Component 2 (FI 120-s) of the multiple schedule. Baseline (mean) and 95% confidence intervals are for preinjection sessions. The baseline for assessing the effects of extinction was the mean of the five sessions prior to the first extinction session.

Component	Rat 87		Rat 89		Rat 66	
	1	2	1	2	1	2
			d-Amphetamine sulfate (mg/kg)			
Baseline	30	19	26	19	28	14
Conf. int.	34–26	22–15	29–22	23–16	32–24	18–11
Drug dose						
0	19	11	28	28	29	15
0	22	12	26	18	15	11
0.125	17	14	29	21	23	15
0.25	24	16	41	30	16	11
0.5	27	10	27	18	16	9
1	14	11	3	7	7	6
1	28	15	4	3	13	8
2	7	8	0	0	8	8
2	7	8	—	—	13	8
			CCK8 (μg/kg)			
Baseline	31	19	24	20	23	14
Conf. int.	36–27	22–17	27–20	24–15	29–17	17–12
Drug dose						
0	34	22	17	8	17	8
0	—	—	20	17	23	18
1	37	18	14	10	28	15
10	35	27	4	4	3	5
10	—	—	23	10	4	4
40	21	17	2	5	3	6
100	39	14	—	—	—	—
100	29	16	—	—	—	—
150	1	2	—	—	—	—
200	0	0	—	—	—	—
			Sodium pentobarbital (mg/kg)			
Baseline	34	18	27	18	31	21
Range[a]	36–30	19–17	36–22	21–14	36–27	26–18
Drug dose						
0	41	19	25	29	27	25
12	8	9	1	5	8	13
24	2	1	1	4	6	9
			Extinction			
Baseline	25.6	15.5	21.8	13.5	25.9	16.7
Conf. int.	28.9–22.3	18.6–12.4	29.0–14.6	19.1–7.9	34.0–17.8	21.1–12.3
Session 1	18.3	6.2	6.1	1.1	26.1	9.4
Session 2	10.1	1.5	0.8	0.3	15.2	2.3
Session 3	3.7	1.0	0.6	0.3	6.7	0.7

[a] The range was used in the sodium pentobarbital condition because the confidence interval was not meaningful with only three baseline scores.

APPENDIX

Table A3

Summary of absolute response rate (responses per min) during sessions following administrations of CCK8, sodium pentobarbital, and *d*-amphetamine for Component 1 (RI 30-s) and Component 2 (RI 120-s) of the multiple schedule. Baseline (mean) and 95% confidence intervals are for preinjection sessions. Baseline for the extinction test is the mean and 95% confidence interval for five reinforcement sessions immediately before the first exposure to the extinction procedure.

Component	Rat 81		Rat 82		Rat 98		Rat 99	
	1	2	1	2	1	2	1	2
				CCK8 (μg/kg)				
Baseline	120	61	107	52	89	35	95	38
Conf. int.	129–110	74–47	135–79	67–37	105–73	42–27	118–72	49–28
Drug dose								
0	120	66	104	50	95	30	108	44
1	—	—	99	39	86	33	110	41
5	124	46	109	38	65	27	50	23
20	36	18	81	35	48	17	33	20
40	3	7	31	16	32	16	37	18
				Sodium pentobarbital (mg/kg)				
Baseline	132	65	83	35	77	33	91	38
Conf. int.	146–119	77–53	90–75	40–29	91–62	37–29	105–78	45–30
Drug dose								
0	117	55	72	37	83	37	92	40
12	107	65	74	29	84	44	56	38
16	115	44	41	23	20	17	90	31
24	61	52	9	7	22	22	20	17
				d-Amphetamine sulfate (mg/kg)				
Baseline	114	62	109	39	81	39	83	39
Conf. int.	119–109	65–58	119–98	44–33	88–75	43–35	90–77	42–35
Drug dose								
0	126	65	104	45	87	35	102	48
0.125	104	54	120	40	92	41	87	31
0.25	91	50	123	43	99	41	87	30
0.5	66	31	122	27	86	30	48	12
0.5	76	45	—	—	—	—	47	16
1	66	41	88	34	77	38	89	36
1	—	—	—	—	—	—	27	19
2	51	31	55	38	88	39	27	19
2	39	31	—	—	—	—	22	26
4	0	0	48	43	80	79	—	—
4	—	—	17	12	16	13	—	—
8	—	—	0	0	47	43	—	—
12	—	—	—	—	0	0	—	—
				Extinction				
Baseline	106.6	62.2	92.4	32.5	71.4	34.8	81.0	36.2
Conf. int.	113.0–100.2	67.2–57.2	111.0–73.8	39.2–25.8	76.7–66.1	39.2–30.4	92.4–69.6	44.0–28.4
Session 1	52.6	19.3	38.5	7.5	16.2	3.9	18.9	7.4
Session 2	17.6	5.6	21.9	3.1	7.1	2.6	5.3	1.3
Session 3	11.9	1.8	20.6	1.8	5.6	0.8	4.8	1.3