JOURNAL OF THE EXPERIMENTAL ANALYSIS OF BEHAVIOR VOLUME 5, NUMBER 1 JANUARY, 1962

EFFECTS OF dl-AMPHETAMINE UNDER CONCURRENT VI DRL REINFORCEMENT

EVALYN F. SEGAL[1]

WALTER REED ARMY INSTITUTE OF RESEARCH AND
LABORATORY OF PSYCHOPHARMACOLOGY, UNIVERSITY OF MARYLAND[2]

Three adult, food-deprived rats were given IP injections of *dl*-amphetamine sulfate under DRL and concurrent VI DRL reinforcement schedules. The drug results were as follows. (1) The IRT distributions of DRL responses shifted to the left, but some temporal discrimination remained. (2) The IRT distributions of VI responses shifted slightly to the left. (3) The distinguishing characteristics of VI and DRL IRT distributions were preserved. (4) The frequency distribution of number of VI responses between two consecutive DRL responses was relatively unaffected. (5) Over-all response rates on the two components of the concurrent schedules increased more or less proportionately.

These findings imply that the primary behavioral effect of *dl*-amphetamine was a motor excitatory one. The drug's disruption of timing behavior was not due to a derangement of internal timing mechanisms, nor to interference with the topography or pattern of behavior. Rather, it might be a secondary result of the accelerated emission of overt behavior patterns mediating the temporal spacing of DRL bar presses.

Several reviews of psychopharmacological research on the amphetamines have appeared within recent years (Brady, 1957; Dews & Morse, 1961; Owen, 1960; Sidman, 1959). From these reviews and the supporting data, some principles of amphetamine action are gradually emerging that promise to unify the vast and paradoxical body of amphetamine findings. The following are among the principles with the best experimental support. (1) Amphetamine reduces food and water consumption (Dews & Morse, 1961) and possibly some vague entity called "appetite" (Owen, 1960). (2) In carefully circumscribed conditions, amphetamine increases the total amount of "spontaneous activity" (Dews & Morse, 1961). (3) Amphetamine enhances "conditioned emotionality,"[3] especially aversively aroused emotionality (Brady, 1957; Teitelbaum & Derks, 1958) and "post-drug depression" (Verhave, 1958), but perhaps also "euphoric" types of emotion (Dews & Morse, 1961; Miller, 1956, 1957). (4) Amphetamine differentially affects behavior maintained by different reinforcement schedules (Dews & Morse, 1961) and by different parameters of a given schedule (Dews, 1960). (5) Amphetamine influences rates of responding both by shortening long (5 sec or more) IRT's and lengthening short (less than 1 sec) IRT's (Dews, 1958; Dews & Morse, 1961; Morse & Herrnstein, 1956).

Another finding, which is not so well confirmed as those above but yet is mentioned in the experimental literature, is that appropriate doses of amphetamine affect discriminative behavior. Apparently, simple discriminations are not affected (Dews, 1955; Sidman, 1956a, 1956b), but complex "conditional" discriminations are (Dews, 1955). Moreover, impairment of "sensory responsiveness" or "attentiveness" is suggested by failure to respond to stimuli signalling the brief availability of food (Teitelbaum & Derks, 1958; Weissman, 1959). The failure of food consumption may, of course, be interpreted simply as a consequence of reduced "hunger." However, as Teitelbaum and Derks (1958) contend, and this writer concurs, animals under amphetamine often

[1]This research was completed during the writer's tenure of a Postdoctoral Research Fellowship from the National Institute of Neurological Diseases and Blindness, under the sponsorship of Dr. J. V. Brady. Thanks are due to the Laboratory of Psychopharmacology of the University of Maryland for provision of some of the research facilities under Grant No. MY-1604 from the National Institute of Mental Health, and to Mr. C. R. Schuster for advice and assistance in the conduct of the experiment.

[2]Present address: San Diego State College.

[3]Dews and Morse (1961) think that the evidence on this point is no more than suggestive; nonetheless, it has sufficient experimental support to qualify as a promising integrative principle.

show a quality of "obliviousness"; they may work at very high response rates, yet fail to respond to food signals.

One area of conflicting data concerns the nature of amphetamine effect on *rate* of responding. Dews and Morse (1961) have noted that amphetamine sometimes increases rates of reinforced responding (*e.g.*, Brady, 1957; Dews & Morse, 1958; Miller, 1956; Morse & Herrnstein, 1956; Sidman, 1955, 1956a, 1956b; Skinner & Heron, 1937; Verhave, 1958; Weissman, 1959; Wentink, 1938) and rates of extinction responding (*e.g.*, Miller, 1956; Skinner & Heron, 1937; Weissman, 1959); amphetamine sometimes decreases response rates (*e.g.*, Dews, 1955, 1958, Miller, 1956; Owen, 1960; Verhave, 1958; Weissman, 1959); and sometimes, as in operant level (Verhave, 1958) and some variable-interval schedules (Dews, 1955, 1958), amphetamine has no appreciable effect on rate of responding. Dews and Morse (1961) explain these disparities by the principle that amphetamine reduces long IRT's (hence tending to increase rate) but lengthens short IRT's (hence tending to decrease rate). To account for Verhave's operant-level data, they add the qualification that the response must at some minimum strength before any amphetamine effect occurs.

This IRT principle of amphetamine action brings some coherency to the confusing welter of contradictory data. Thus, Dews and Morse are able to explain the dependency of amphetamine effects on reinforcement schedule in terms of the type of IRT distribution generated by the schedule. Among other implications, their position makes dubious the view that amphetamine-induced changes in DRL performance are due to a specific disruption of timing mechanisms. Dews and Morse interpret the DRL result as simply one among many similar effects on IRT's common to many reinforcement schedules and not specifically related to temporal factors.

Possibly amphetamine, like many other independent variables, may selectively and differentially affect various dimensions of a single response class, or various components of an organism's response repertoire. Several authors have lately argued, in other contexts, for the examination of other dimensions of response besides rate (*e.g.*, Herrnstein, 1961; Millenson & Hurwitz, 1961; Notterman, 1959), and for the consideration of larger portions of the response repertoire (Bindra, 1961) and the interrelations among components of the repertoire having differing probabilities of emission (Premack, 1959, 1961). Segal (1959) has suggested that food-and water-deprivation might differentially affect responses which are already at high strength; and this suggestion is equally relevant to other experimental variables. It is reminiscent of Dews and Morse's (1961) explanation for the lack of amphetamine effect on operant level. The converse is equally likely, namely, that some independent variables may differentially affect responses which are at low strength. Premack (1961) and Premack and Collier (1961) have made a similar proposal in differentiating between "recurrent" and "nonrecurrent" responses; they suggest that many experimental variables may have differential effects upon these two classes of behavior. Dews (1960) has presented supporting evidence, in the form of inverse functional relations between pentobarbitial- and amphetamine-induced rate increases, and control response rate. Finally, there may be complex interactions, such that responses at high strength are altered in one direction and responses at low strength are altered in the opposite direction, by one and the same experimental treatment.[4] This is closely related to Dews and Morse's description of amphetamine effects on IRT, but the principle may extend to other independent variables besides amphetamine.

In the present experiment, I examined the effects of amphetamine on characteristic IRT distributions generated by the two components of a concurrent schedule. The experiment was designed around the following facts. (a) Food-motivated, variable-interval responding is characterized by a monotonically decreasing IRT distribution (Anger, 1956). (b) Variable-interval responding increases or decreases under amphetamine, presumably as a function of the proportion of long and short IRT's in the control (saline or nondrug) sessions (Dews, 1958). (c) Food-motivated DRL schedules of reinforcement generate a characteristic bimodal IRT distribution, with one mode at the shortest recorded IRT interval, and a second mode at or near the minimum reinforceable IRT interval (Sidman, 1955, 1959). (d) Amphetamine causes an increase in over-all

[4]Dr. Ardie Lubin (personal communication) has given the name "disordinal interaction" to such cases.

DRL response rate, accompanied by a shift in the second IRT mode toward shorter IRT's (Sidman, 1955, 1959).

In spite of the shifts toward shorter IRT's, DRL behavior under amphetamine shows evidence that *some* temporal discrimination is retained: The IRT distribution remains bimodal (Sidman, 1959). This is in line with Dews and Morse's (1961) argument; the disruption of timing behavior caused by amphetamine may be the simple result of shortening in long IRT's, or "motor excitation," and not a specific derangement of temporal discrimination.

The present experiment tests this notion under conditions of concurrent VI DRL reinforcement on two levers. If amphetamine similarly affects the IRT distributions of both response classes, it will confirm Dews and Morse's position.

METHOD

The subjects were three adult, male, albino rats, deprived to 80% of free-feeding weight. The apparatus was a two-lever Foringer enclosure, located in an air-conditioned, sound-resistant experimental room, and isolated from programming and recording equipment. The reinforcer was diluted condensed milk, delivered *via* a dipper which rested in the *down* position when not energized. A buzzer sounded throughout the dipper-operation, up-down cycle.

Following a day of magazine training, the animals were placed on a DRL 16-sec reinforcement schedule on one lever, and kept on this procedure for 54 daily sessions. The second lever was inoperative at this time. Beginning with the 25th session, *dl*-amphetamine sulfate ("Benzedrine") was administered intraperitoneally in physiological saline from time to time. At least two nondrug days intervened between drug administrations, and drug was never given oftener than twice in 1 week. Five saline sessions preceded the first drug session. Thereafter, a day of saline always preceded a day of amphetamine, and served as a control for drug observations. On all injection days, the animals were placed in the experimental apparatus and the session begun immediately following injection.

Drug dosages from 0.5 mg/kg to 2.5 mg/kg were given in mixed order during this stage of the experiment. Finally, a single dosage was selected for each animal which produced easily observable, but not extreme, behavioral effects. For Rats No. 1 and No. 3, this dosage was 1.0 mg/kg; and for Rat No. 2, it was 1.5 mg/kg. Only this "moderate" dosage was used thereafter, in this and succeeding stages of the experiment.

Following the 54th session on DRL 16, a concurrent, 3-min, variable-interval schedule of food reinforcement was introduced on the second lever. Amphetamine was administered twice during concurrent VI 3 DRL 16, on the 24th and 28th daily sessions of the new procedure.

After the 28th session on concurrent VI 3 DRL 16, the schedule on the second lever was changed to VI 1 min, and amphetamine was administered twice, on the 30th and 35th sessions of this final procedure.

Saline and noninjection sessions were run until 150 food reinforcements had been given; drug sessions were run either to 150 reinforcements or until 100 min had elapsed, whichever occurred first.

RESULTS

Figure 1 shows saline and drug IRT distributions under the DRL schedule, for each stage of the experiment. The distributions were computed from the data of complete sessions. No systematic differences in the IRT distributions as a function of pairing with a concurrent VI schedule were apparent in these sessions.[5]

In all cases, the effect of drug was to shift the IRT distributions toward shorter intervals. Temporal patterning of DRL responses was not completely lost, however. In most of the drug IRT distributions in Fig. 1, the responses tended to be spaced farther apart than the minimum (0-4 sec) recorded interval. In fact, the proportion of DRL responses spaced less than 4 sec apart was not markedly affected by drug. Rather, the primary effect was on the proportion of responses spaced far enough apart to earn reinforcement, that is, 16 sec or more. These data support Dews and Morse (1961), who set the critical limits

[5]Interactions between the components of a concurrent VI DRL schedule occur early in exposure to the schedule (Segal, 1961), but disappear after prolonged exposure.

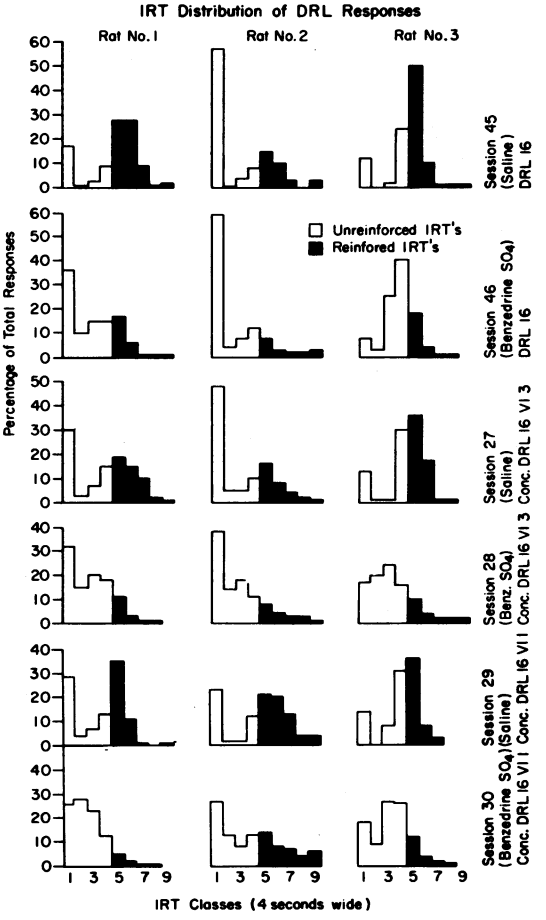

Fig. 1. Inter-response-time distributions of responses on the DRL lever for selected saline and drug sessions.

for amphetamine effects at IRT's longer than about 5 sec or shorter than about 1 sec.

Figure 2 shows saline and drug IRT distributions on the VI lever under concurrent VI 3 DRL 16 and concurrent VI 1 DRL 16. Again, the distributions were computed from data for complete sessions, and represent stabilized behavior after extended exposure to the experimental conditions.

The variable-interval reinforcement contingencies generated moderately high rates of responding. This is reflected in the unimodal character of the IRT distributions, with the single mode at the shortest recorded IRT interval. The effect of amphetamine was a very slight shift to the left in the distributions. The proportion of responses at the shortest IRT interval was not markedly changed, but the proportion of responses spaced 4-12 sec apart was increased, relative to the proportion of still longer IRT's. These effects occurred for all animals, in spite of marked disparities between the characteristic forms of their respective IRT distributions. Again, the result confirms Dews and Morse's (1961) description of amphetamine action on VI responding.

Figure 3 shows frequency distributions of the number of responses occurring on the VI lever between each two consecutive responses on the DRL lever. These plots reflect patterning of switches *between* the two levers. The modes at zero VI responses between two

Table 1

Ratio of Bar-pressing Rate under *dl*-amphetamine to Bar-pressing rate on the Preceding Physiological Saline Session ("Output Ratio")

Procedure	*Rat No. 1*		*Rat No. 2*		*Rat No. 3*	
	DRL Lever	*VI Lever*	*DRL Lever*	*VI Lever*	*DRL Lever*	*VI Lever*
DRL 16:						
Drug, Session 46 / Saline, Session 45	1.96	—	1.27	—	1.29	—
VI 3 DRL 16:						
Drug, Session 24 / Saline, Session 23	1.51	2.57	1.33	1.42	1.22	1.52
Drug, Session 28 / Saline, Session 27	1.60	1.83	1.07	1.07	1.50	0.94
VI 1 DRL 16:						
Drug, Session 30 / Saline, Session 29	1.71	1.72	1.27	1.29	1.37	1.09
Drug, Session 35 / Saline, Session 34	1.38	1.34	1.40	1.23	1.40	0.96

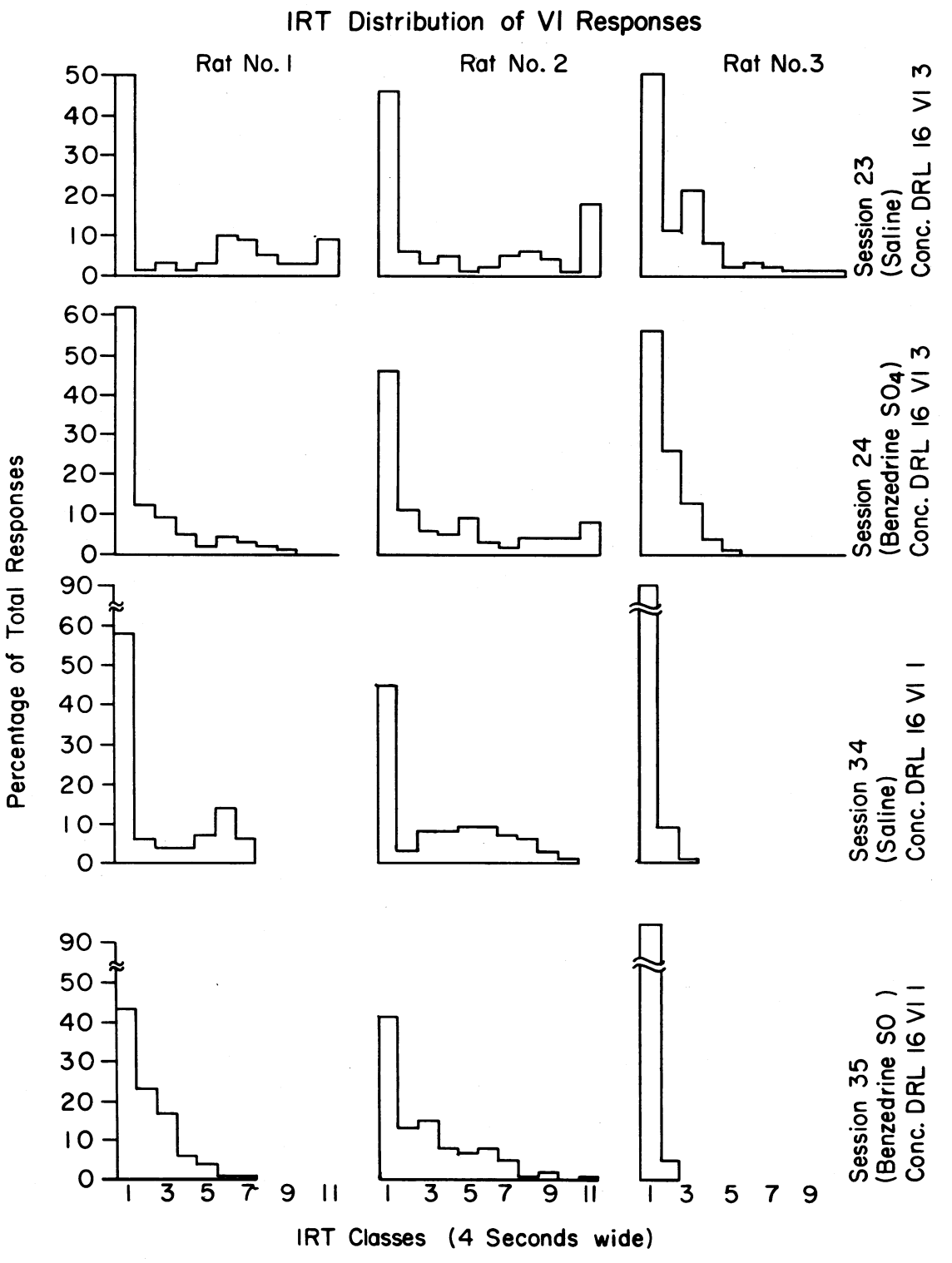

Fig. 2. Inter-response-time distributions of responses on the VI lever for selected saline and drug sessions.

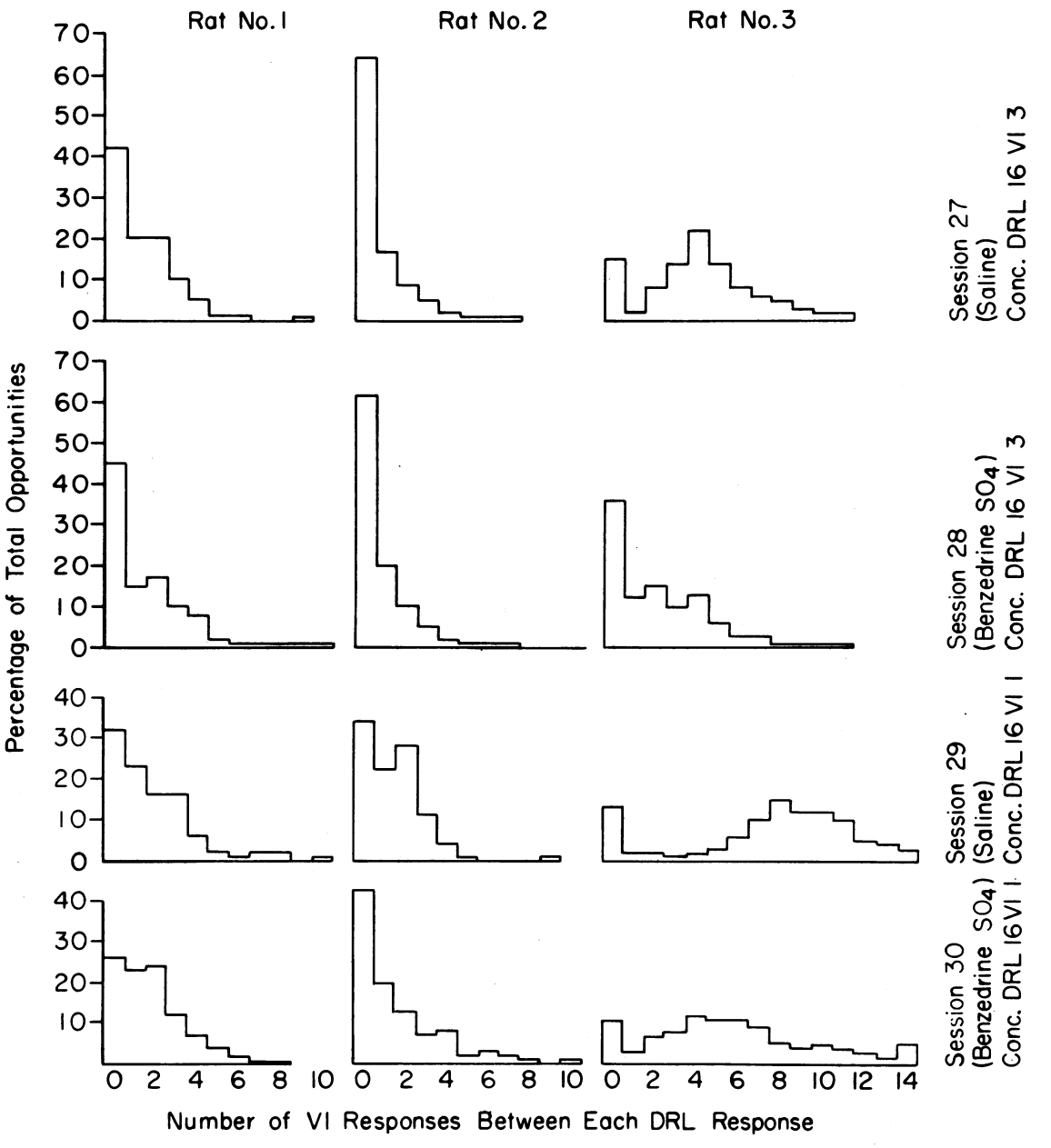

Fig. 3. Frequency distributions showing number of responses on the VI lever between each two consecutive responses on the DRL lever, for selected saline and drug sessions.

consecutive DRL responses are the consequence of fast "bursts" of DRL responses.

Whatever the pattern of responding between the two levers for individual animals, it was relatively unaffected by amphetamine. The records for Rats No. 1 and No. 2 show no marked differences between saline and drug days. However, Rat No. 3 shifted slightly toward fewer VI responses between DRL responses under drug.

Table 1 shows the changes in rate of bar pressing on each lever as a result of amphetamine, expressed as a ratio of the rate on the drug day to the rate on the preceding saline day [what Dews (1955) has called the "output ratio"]. The rates in the computations were

not corrected for eating time. Ratios above 1.00 indicate drug-induced increases in response rate, and ratios below 1.00 indicate drug-induced decreases. For the first stage of the experiment, simple DRL on one lever, only the results for the reinforced, DRL lever are shown.

Of the 27 ratios computed, 22 reflect drug-induced rate increases of at least 22%; 3 reflect increases of 7-9%; and 2 reflect rate decreases of 4-6%. Rate changes under 10% may reasonably be dismissed as insignificant, leaving the conclusion that at the dosages given, amphetamine either increased over-all response rates or left them unaffected. The drug produced no significant decreases in rate.

There was no systematic interaction of the drug effect with the schedule of reinforcement. For the most part, drug increased rates of bar pressing about as much or as little under simple DRL and concurrent VI DRL.

Incidental observation of the animals during drug sessions indicated that they did not always drink the milk reinforcer on these days. Yet, responding continued unabated throughout drug sessions. No failures to consume the milk on nondrug days were noted. These observations confirm the many previous reports of reduced consumption of freely available food (Dews & Morse, 1961), as well as reports of failures to consume liquid food reinforcers in a bar-pressing apparatus under amphetamine (Teitelbaum & Derks, 1958; Weissman, 1959).

DISCUSSION

The data confirm previous findings that some temporal discrimination is retained under amphetamine. Even under drug, the temporal patterning of responses on the two levers continued to be markedly different. The VI responding, which showed no temporal spacing under saline, *a fortiori* showed none under drug. The DRL responding, which did show temporal patterning under saline, continued to show it under drug, although the efficiency of temporal spacing with respect to the reinforcement contingencies was impaired.

The finding that amphetamine affected response rates on the two components of the concurrent schedule about equally indicates that the main effect of the drug was apparently a motor excitatory one, and not a specific disruption of some *internal* timing mechanism. This is completely consistent with Dews and Morse's (1961) contention that amphetamine simply reduces the long IRT's of DRL (and other) reinforcement schedules.

The precise mediating factors in temporal discrimination are not well understood. The present findings support the interpretation that other overt behavior, consisting of some regular cycle performance, may intervene between DRL responses and mediate the temporal spacing of DRL responding. The fact that the pattern of responding *between* the two levers was relatively unaffected by amphetamine is consistent with such an interpretation: The cycle of behavior on the two levers, including switching between them, was simply run off faster under drug. To the extent that *overt* behavior mediates timing behavior, then amphetamine may be said to disrupt temporal discrimination. But this is a secondary effect, produced not by interference with an internal timing mechanism, but rather by increasing the rate of emission of all overt behavior.

Of course, internal timing mechanisms still may exist. Brady and Conrad (1960) have demonstrated that intracranial self-stimulation (ICS) of the globus pallidus causes an interference with timing behavior similar to that produced by amphetamine. Moreover, their data strongly suggest a precisely localized neural timing mechanism, because ICS in the medial forebrain bundle (MFB) or the thalamus did not share the disruptive effect of globus pallidus stimulation on DRL performance.

The fact that DRL behavior is similarly disrupted by amphetamine and by ICS in the globus pallidus does not argue that the mode or site of action of these two treatments is necessarily the same. On the contrary, several lines of evidence make such a conclusion dubious. Miller (1957) has reported that amphetamine increases the speed of bar pressing to turn on ICS of the MFB, at the same time decreasing speed of bar pressing to turn off the stimulation. Two investigators (reviewed in Dews & Morse, 1961) have found that amphetamine-induced suppression of feeding is exaggerated in hypothalamic hyperphagics. Finally, Brady and Conrad (1960) report that the rate of VI (*but not DRL*)

responding is higher when the reinforcement is MFB stimulation than when it is sugar pellets. Taken together, these findings suggest that amphetamine's neural action may be upon motivational mechanisms located in the hypothalamus. They offer no evidence of an amphetamine effect directly on the globus pallidus, where Brady and Conrad have localized a timing mechanism. These data do not strictly rule out the possibility that amphetamine may act upon the hypothalamus *via* the basal ganglia, but neither do they provide any support for such a contention. On present evidence, then, amphetamine action and timing mechanisms appear to be neurally independent.

The failure of food consumption in the apparatus on drug days may be interpreted either as a reduction in "hunger motivation," or as a result of the motor excitation induced by amphetamine: The animals may have been "too busy" pressing the levers to respond promptly and efficiently to the sound of the buzzer associated with the brief availability of the milk dipper in the *up* position. As mentioned earlier, it is not likely that the effect is on simple discriminative capacity, but it might represent a derangement in "attention."

REFERENCES

Anger, D. The dependence of inter-response-times upon the relative reinforcement of different inter-response-times. *J. exp. Psychol.*, 1956, **52**, 145-161.

Bindra, D. Components of general activity and the analysis of behavior. *Psychol. Rev.*, 1961, **68**, 205-215.

Brady, J. V. A review of comparative behavioral pharmacology. *Ann. N.Y. Acad. Sci.*, 1957, **66**, 719-732.

Brady, J. V., and Conrad, D. G. Some effects of brain stimulation on timing behavior. *J. exp. Anal. Behav.* 1960, **3**, 93-106.

Dews, P. B. Studies on behavior. II. The effects of pentobarbital, methamphetamine and scopolamine on performances in pigeons involving discriminations. *J. pharmacol. exp. Therap.* 1955, **115**, 380-389.

Dews, P. B. Studies on behavior. IV. Stimulant actions of methamphetamine. *J. pharmacol. exp. Therap.* 1958, **122**, 137-147.

Dews, P. B. Free-operant behavior under conditions of delayed reinforcement. I. CRF-type schedules. *J. exp. Anal. Behav.*, 1960, **3**, 221-234.

Dews, P. B., and Morse, W. H. Some observations on an operant in human subjects and its modification by dextroamphetamine. *J. exp. Anal. Behav.*, 1958, **1**, 359-364.

Dews, P. B., and Morse, W. H. Behavioral pharmacology. *Ann. Rev. Pharmacol.*, 1961, **1**, 145-174.

Herrnstein, R. J. Stereotypy and intermittent reinforcement. *Science*, 1961, **133**, 2067-2069.

Millenson, J. R., and Hurwitz, H. M. B. Some temporal and sequential properties of behavior during conditioning and extinction. *J. exp. Anal. Behav.*, 1961, **4**, 97-106.

Miller, N. E. Effects of drugs on motivation: the value of using a variety of measures. *Ann. N. Y. Acad. Sci.*, 1956, **65**, 318-333.

Miller, N. E. Experiments on motivation. *Science*, 1957, **126**, 1271-1278.

Morse, W. H., and Herrnstein, R. J. Effects of drugs on characteristics of behavior maintained by complex schedules of intermittent positive reinforcement. *Ann. N. Y. Acad. Sci.*, 1956, **65**, 303-317.

Notterman, J. M. Force emission during bar pressing. *J. exp. Psychol.*, 1959, **58**, 341-347.

Owen, J. E., Jr. The influence of *dl*-, *d*-, and *l*-amphetamine and *d*-methamphetamine on a fixed-ratio schedule. *J. exp. Anal. Behav.*, 1960, **3**, 293-310.

Premack, D. Toward empirical behavior laws. I. Positive reinforcement. *Psychol. Rev.*, 1959, **66**, 219-233.

Premack, D. Predicting instrumental performance from the independent rate of the contingent response. *J. exp. Psychol.*, 1961, **61**, 163-171.

Premack, D., and Collier, G. Analysis of nonreinforcement variables affecting response probability. *Psychol. Monogr.*, in press.

Segal, Evalyn F. Confirmation of a positive relation between deprivation and number of responses emitted for light reinforcement. *J. exp. Anal. Behav.*, 1959, **2**, 165-169.

Segal, Evalyn F. Behavioral interaction under concurrent spaced-responding, variable-interval schedules of reinforcement. *J. exp. Anal. Behav.*, 1961, **4**, 263-266.

Sidman, M. Technique for assessing the effects of drugs on timing behavior. *Science*, 1955, **122**, 925.

Sidman, M. Time discrimination and behavioral interaction in a free operant situation. *J. comp. physiol. Psychol.*, 1956, **49**, 469-473. (a)

Sidman, M. Drug-behavior interaction. *Ann. N. Y. Acad. Sci.*, 1956, **65**, 282-302. (b)

Sidman, M. Behavioral pharmacology. *Psychopharmacologia*, 1959, **1**, 1-19.

Skinner, B. F., and Heron, W. T. Effects of caffeine and Benzedrine upon conditioning and extinction. *Psychol. Rec.*, 1937, **1**, 340-346.

Teitelbaum, P., and Derks, P. The effect of amphetamine on forced drinking in the rat. *J. comp. physiol. Psychol.*, 1958, **51**, 801-810.

Verhave, T. The effect of methamphetamine on operant level and avoidance behavior. *J. exp. Anal. Behav.*, 1958, **1**, 207-219.

Weissman, A. Differential drug effects upon a three-ply multiple schedule of reinforcement. *J. exp. Anal. Behav.*, 1959, **2**, 271-287.

Wentink, E. The effects of certain drugs and hormones upon conditioning. *J. exp. Psychol.*, 1938, **22**, 150-163.

Received April 27, 1961