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BEHAVIORAL PARAMETERS OF DRUG ACTION: SIGNALLED AND RESPONSE-INDEPENDENT REINFORCEMENT[1]

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Four pigeons were initially trained under a multiple variable-interval 1-min variable-interval 1-min schedule of food reinforcement. For two of the pigeons, a signal was then presented whenever the reinforcer was available in one component; this resulted in positive contrast. For the other two pigeons, the reinforcer was presented independently of responding on a variable-time schedule in one component; this resulted in negative induction. After 30 to 50 sessions, however, a similar degree of differential responding occurred under both multiple schedules, *i.e.*, high rates in the variable-interval component and low rates in the other component. Reinforcement frequency remained about the same in each of the schedule components. The stable performances then served as baselines for studying drug effects. In the high-rate component of both multiple schedules, small doses of *d*-amphetamine increased responding, whereas larger doses decreased responding. In the low-rate component of both multiple schedules, there was no rate-increasing effect at any dose of *d*-amphetamine; such an effect was found, however, with phenobarbital at a dose that decreased responding in the high-rate component. The drug effects thus depended on the interaction of pharmacologic variables (specific drug and dose) with behavioral variables (schedule components).

In some recent experiments using multiple schedules of food presentation with pigeons, differential responding was established under conditions in which the rate of reinforcement was constant (Boakes, 1973; Brownstein and Hughes, 1970; Halliday and Boakes, 1971, 1972; Weisman and Ramsden, 1973; Wilkie, 1972, 1973). Initially, responding was reinforced on a multiple schedule consisting of two identical variable-interval components (*mult* VI VI). Differential responding was then established in one of two ways. In the method used by Brownstein and Hughes (1970) and Wilkie (1973), a signal was presented whenever the reinforcer was available in one component (*mult* VI VI + signal). In the other method (Boakes, 1973; Halliday and Boakes, 1971, 1972; Weisman and Ramsden, 1973; Wilkie, 1972), the reinforcer was presented independently of responding on a variable-time schedule in one component (*mult* VI VT). In both methods, the response rate in the changed component (VI + signal or VT) usually decreased substantially even though the rate of reinforcement remained constant. The response rate in the unchanged component (VI) tended to increase under *mult* VI VI + signal (*i.e.*, "positive contrast" occurred) but remained relatively constant or decreased slightly ("negative induction") under *mult* VI VT.

The first objective of the present research was to replicate the above findings. The second objective was to use *mult* VI VI + signal and *mult* VI VT as baselines for studying drug effects. The major focus was on the effects of varying doses of *d*-amphetamine. This drug has been widely studied with multiple fixed-ratio fixed-interval schedules and these studies have usually concluded that certain doses increase low rates of responding while decreasing high rates (see reviews by Grossman and Sclafani, 1971; Kelleher and Morse, 1968; Weiss and Laties, 1969). There has been, however, one enduring problem in many of the experiments showing such "rate-dependent" drug effects, namely, ". . . that of manipulating rate while keeping constant other potentially important variables, such as reinforce-

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ment density and schedule of reinforcement (Weiss and Laties, 1969, p. 319)." The present research attempted to deal with this problem by using multiple schedules that generated different rates of responding under conditions in which the rate of reinforcement was constant. Finally, to provide an additional comparison, a single dose of phenobarbital (40 mg/kg) was also tested.

METHOD

Subjects

Four adult male White King pigeons, experimentally naive at the start of the research, were maintained within 10 g of 80% of their free-feeding weights by food presented during the sessions and by post-session supplemental feeding. The 80% values ranged between 464 and 504 g. Water and grit were always available in the home cages.

Apparatus

The apparatus consisted of a standard two-key pigeon chamber (BRS-Foringer PH-001) and connecting automatic control equipment. A minimum force of 15 g (0.15 N) was required to operate the right response key, which could be transilluminated by red, green, or white light; the left key was dark and inoperative throughout the experiment. The houselight was two shielded white lamps mounted directly above the keys near the ceiling. Scheduling of events was accomplished by means of timers, steppers, and associated relay circuitry; the recording was by counters and a cumulative recorder. White noise was continuously present in the chamber to mask extraneous sounds.

Procedure

Throughout the following procedures the reinforcer was 4-sec access to mixed grain. Presentation of the food magazine was accompanied by the offset of the keylight and the onset of the magazine light. A "blackout" (all lights off) of variable duration preceded and followed each session. With few exceptions, there were seven daily sessions a week.

Preliminary training. The first session consisted of magazine training, shaping of key pecking (*cf.* Ferster and Skinner, 1957), and reinforcing each response (continuous reinforcement, CRF) for 40 reinforcements. During response shaping and the first 20 reinforcements, the keylight was white. During the next 20 reinforcements, a multiple schedule (*mult* CRF CRF) was in effect and the keylight alternated between red and green after every five reinforcements.

During the last phase of preliminary training (20 sessions for Pigeon 1772; 10 sessions for each of the other three subjects), responding was reinforced according to a multiple variable-interval 1-min variable-interval 1-min schedule (*mult* VI 1-min VI 1-min). Under this schedule, the keylight alternated between red and green every 5 min and responses in the presence of each color were reinforced after variable intervals averaging 1 min. The interreinforcement intervals in both colors were derived from an arithmetic series of 13 intervals ranging from 0 to 120 sec. Each session began with the red keylight and ended after six presentations of each schedule component (60 min). Throughout the preliminary training, the houselight was always on during each session.

Baseline conditions. The baseline training for Pigeons 3876 and 3713 consisted of 40 sessions in which the reinforcer was signalled in the green component (*mult* VI 1-min VI 1-min + signal). When the keylight was green, the houselight was turned off whenever the reinforcer was available; the houselight was turned on with the next response, which was reinforced by food presentation. When the keylight was red, the houselight was always on.

During the baseline training for the other two subjects (50 sessions for Pigeon 1772; 30 sessions for Pigeon 1600), food was presented according to a variable-interval schedule in the red component and according to a variable-time schedule in the green component (*mult* VI 1-min VT 1-min). Thus, when the keylight was green, food was presented at the same temporal intervals as in VI 1-min but independently of responding. There was no signal for the response-independent reinforcement; the houselight was always on during each session.

In all other aspects (red and green alternating every 5 min, 60-min session, *etc.*), both types of baseline training were identical to the last phase of preliminary training.

Drug testing. After baseline training, the next 10 weeks were used to test the drugs,

d-amphetamine sulfate and phenobarbital sodium. The daily sessions of *mult* VI 1-min VI 1-min + signal and *mult* VI 1-min VT 1-min continued throughout this period. Four doses of *d*-amphetamine (0.5, 1, 2, and 4 mg/kg) and one dose of phenobarbital (40 mg/kg) were tested, and two determinations for each dose were taken with each subject. The drug testing followed the design APAP, where A represents a block of the four doses of *d*-amphetamine (within each block, the doses were tested in a random order) and P represents the single dose of phenobarbital. The drugs were dissolved in saline and injected into the pectoral muscles 5 min before the test sessions, which took place once a week. Another session in each week was preceded by the administration of saline. The volume of each injection was 0.1 ml/100 g body weight.

RESULTS

Figure 1 shows the overall rate of responding per session in each component of the different multiple schedules before the drug testing began. At the end of preliminary training (*mult* VI VI), there was little difference between the response rates in the two schedule components. This non-differential responding was found with all four subjects, despite the fact that there were individual differences in the final level at which the response rates stabilized. During baseline training for Pigeons 3876 and 3713 (*mult* VI VI + signal), the rate of responding in the VI + signal component gradually decreased across sessions and then stabilized at a relatively low level. Note that this level was consistently above zero (about one response per minute or one response per signalled reinforcement). During the period when the response rate decreased in the VI + signal component, the rate in the VI component tended to increase across sessions for both subjects; *i.e.*, "positive contrast" occurred. The VI rate then seemed to stabilize at a relatively high level. During the baseline training for Pigeons 1772 and 1600 (*mult* VI VT), the rate of responding in the VT component gradually decreased to zero and tended

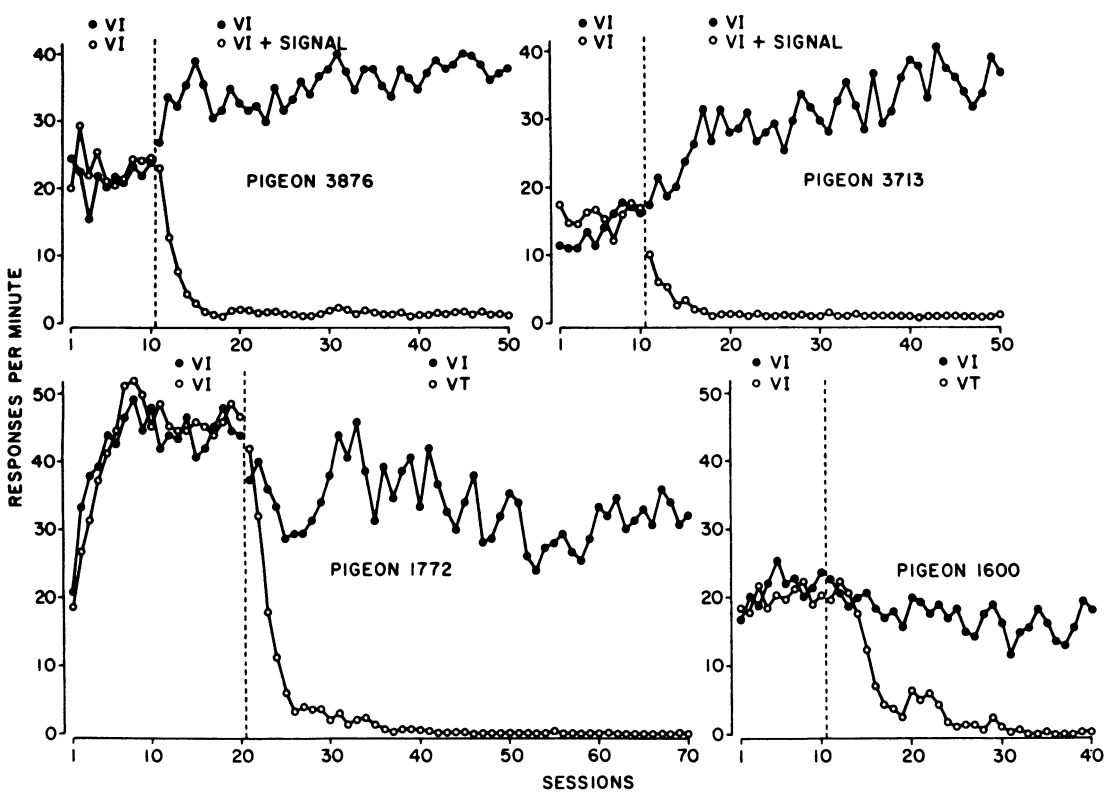

Fig. 1. Overall rate of responding per session in each of the schedule components during preliminary training (*mult* VI VI) and the two types of baseline training (*mult* VI VI + signal and *mult* VI VT).

to remain at this level. The marked decrease in the VT rate was accompanied by a slight downward trend in the VI rate; *i.e.*, "negative induction" occurred. The baseline data are consistent with previous studies of responding under *mult* VI VI + signal (Brownstein and Hughes, 1970; Wilkie, 1973) and *mult* VI VT schedules (Boakes, 1973; Halliday and Boakes, 1971; Weisman and Ramsden, 1973).

In summary, although some apparent behavioral differences (*e.g.*, contrast *versus* induction) emerged during the two types of baseline training, the behavioral similarities were even more striking. A large degree of differential responding was obtained during both types of baseline training. Shifting the schedule from *mult* VI VI to *mult* VI VI + signal or to *mult* VI VT eventually resulted in a response rate in the changed component that was substantially less than the rate in the unchanged component. This was true despite the fact that the reinforcement frequency was about the same in each of the schedule components (28 to 33 reinforcements per session) under both multiple schedules throughout baseline training.

Figure 2 shows the effects of the four doses of *d*-amphetamine and the 40 mg/kg dose of phenobarbital (both determinations) on the overall rate of responding per session in each component of *mult* VI VI + signal (Pigeons 3876 and 3713) and *mult* VI VT (Pigeons 1772 and 1600). The drug data for individual subjects were analyzed by comparing a given drug session with the saline sessions and all of the baseline sessions during drug testing except the one after the drug session. The brackets indicate the ranges of variability for the baseline (B) and saline (S) sessions. A drug was considered to have an effect on response rate to the extent that the dose data fell outside of both ranges (the two dashed horizontal lines).

In general, Figure 2 shows that the drug effects depended on the interaction of pharmacologic variables (specific drug and dose) with behavioral variables (schedule components). In the VI component, some of the smaller doses of *d*-amphetamine increased the rate of responding for all four pigeons; the specific doses that produced this rate enchancement varied with the individual subject. At the larger doses of *d*-amphetamine, however, the VI response rate decreased to below control values. In the other schedule component (VI

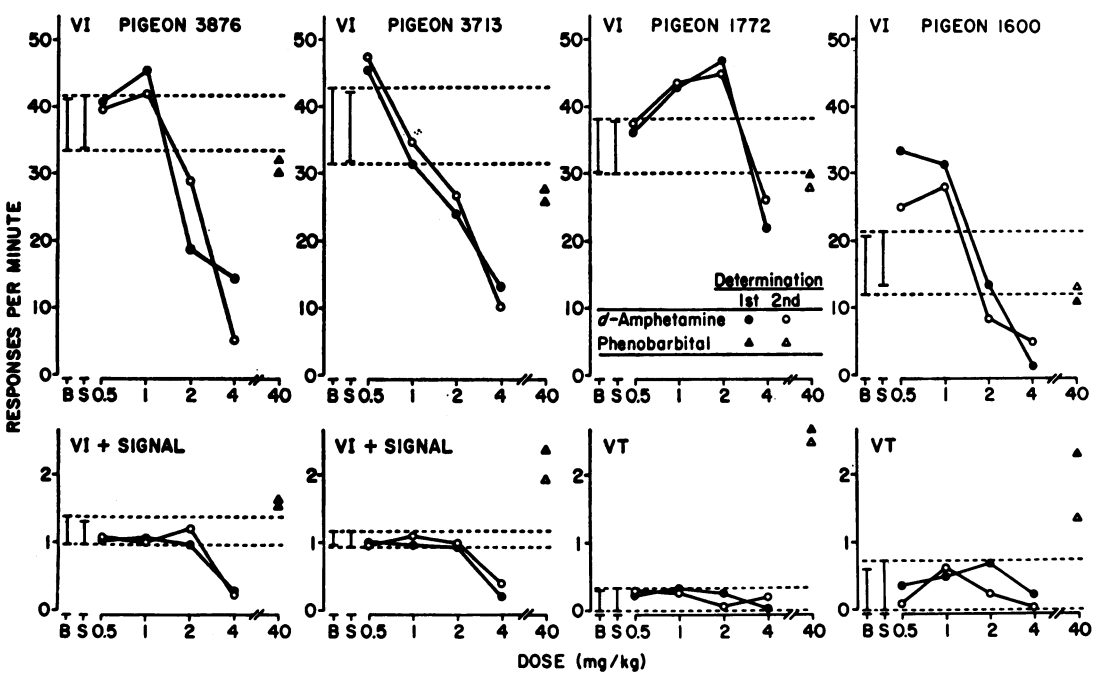

Fig. 2. Effects of *d*-amphetamine and phenobarbital on the overall rate of responding per session in each component of *mult* VI VI + signal and *mult* VI VT. Four doses of *d*-amphetamine and a single dose of phenobarbital were tested and there were two determinations for each dose with each pigeon. The brackets and dashed horizontal lines indicate the ranges of variability for the baseline (B) and saline (S) sessions.

+ signal or VT), there was no rate enhancement at any dose of *d*-amphetamine; the only effect was a decrease in responding at the largest dose (4mg/kg) in the VI + signal component. In contrast to the effects of *d*-amphetamine, phenobarbital (40 mg/kg) increased the response rate in both the VI + signal and VT components. This rate enhancement was accompanied by a slight decrease in the VI response rate for all four pigeons. The first and second determinations of the drug effects generally yielded similar results.

Figure 3 (*mult* VI VI + signal) and Figure 4 (*mult* VI VT) show cumulative response records for representative saline sessions and several drug sessions (first determinations). In general, the within-session control performances (saline sessions) were similar for the two multiple schedules. Each cycle of both multiple schedules was characterized by a high response rate in the VI component and a low response rate in the other component (VI + signal or VT). An apparent difference between the control performances under the two multiple schedules was in terms of post-reinforcement response bursts, which occurred only under *mult* VI VT (both components). Note that the reinforcement frequency was similar in all schedule components.

Figures 3 and 4 also show that the within-session drug effects were similar for the two multiple schedules. In both cases, the rate-increasing effect of the smaller doses of *d*-amphetamine (0.5 mg/kg for Pigeon 3713 and 2 mg/kg for Pigeon 1772) on responding in the VI component did not become apparent until the second or third cycle of the multiple schedule and this effect persisted throughout the remaining VI components. In both cases, the rate-decreasing effect of the largest dose of *d*-amphetamine (4 mg/kg) on VI responding was greatest during the second cycle and responding in most of the subsequent VI components occurred at a reduced rate. Finally, in both cases, the differential effects of phenobarbital (40 mg/kg) were apparent during the

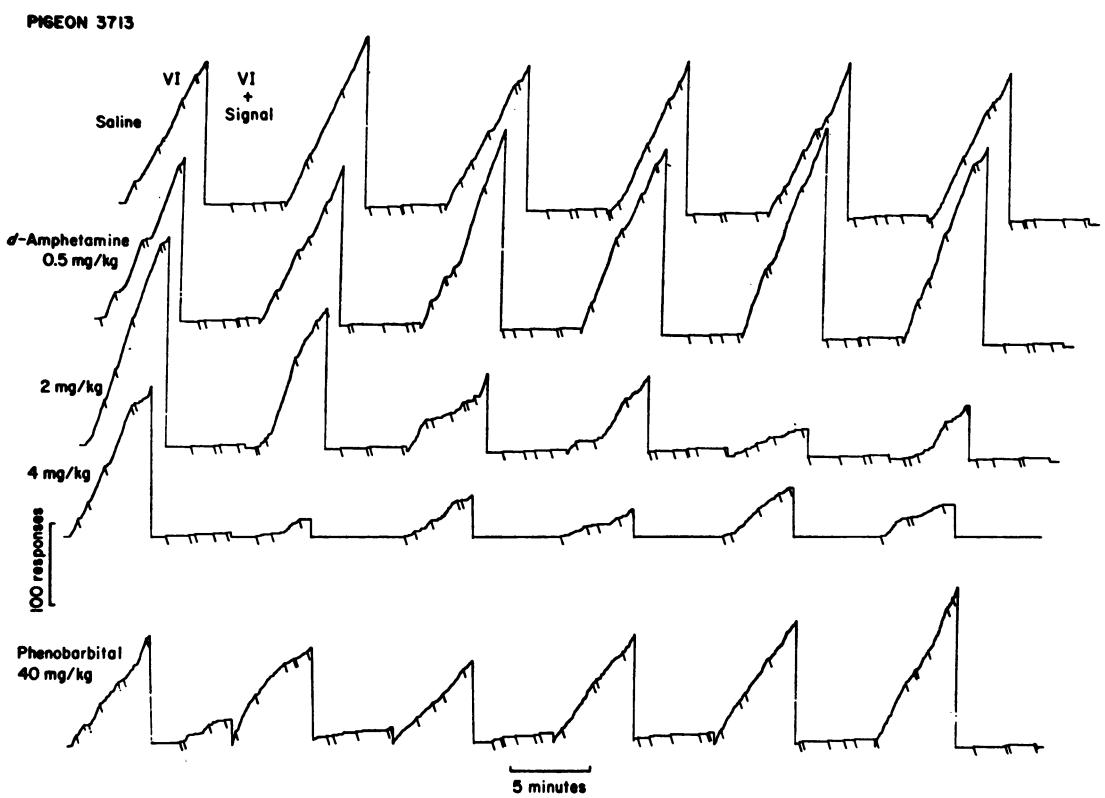

Fig. 3. Cumulative response records for Pigeon 3713 for a saline session and for several drug sessions under *mult* VI VI + signal. Each session began with the VI component and the two components alternated every 5 min. The response pen reset at the end of each schedule component. Reinforcements are indicated by the momentary downward deflection of the response pen.

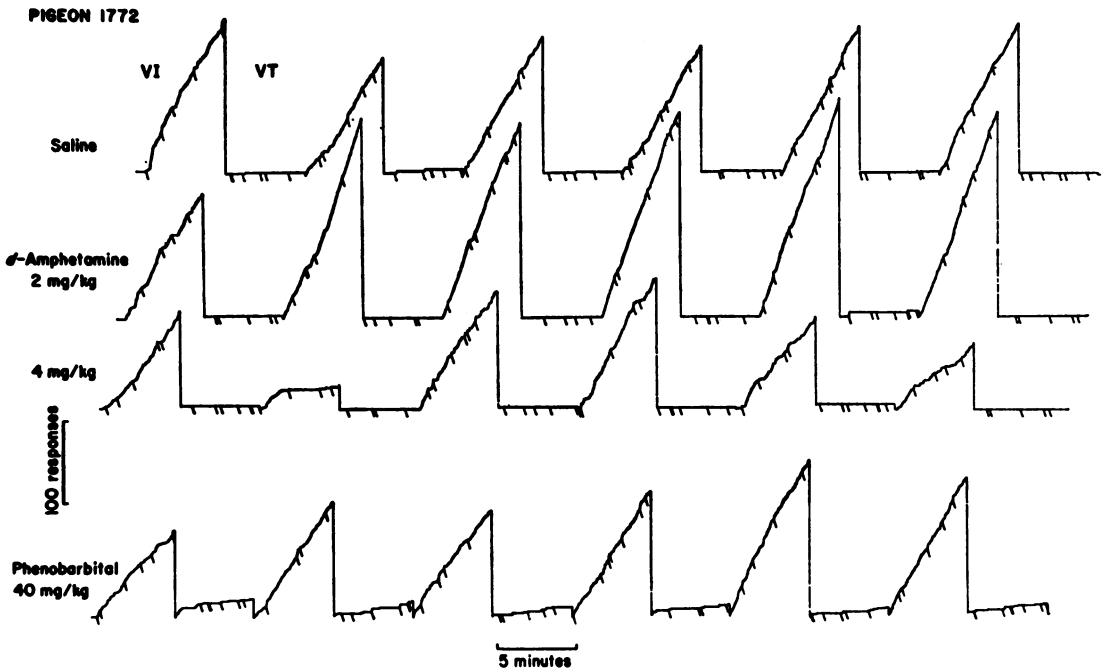

Fig. 4. Cumulative response records for Pigeon 1772 for a saline session and for several drug sessions under *mult* VI VT. Each session began with the VI component and the two components alternated every 5 min. The recording details are the same as in Figure 3.

first cycle (*i.e.*, the normally high rate of responding in the VI component was decreased, whereas the normally low rate of responding in the other component was increased) and both effects tended to disappear as the session progressed. Note that the reinforcement frequency was similar in all schedule components under all drug conditions, except in VI + signal under 4 mg/kg of *d*-amphetamine, where there was no responding at all after the first cycle. Responding in this component was not affected by the 2 mg/kg dose during any part of the session, even though there were both rate-increasing and rate-decreasing effects in the VI component (Figure 3).

DISCUSSION

The data obtained during drug testing indicated that in the VI component of both multiple schedules, low doses of *d*-amphetamine increased response rate, whereas higher doses decreased response rate (Figures 2, 3, and 4). Similar dose-effect data have been obtained with methamphetamine for pigeons under a VI 1-min schedule (Dews, 1958). Different drug effects were found in the Dews (1958) study, however, with a modified fixed-ratio schedule (FR 900). Under this schedule, which generated a relatively low overall response rate under control conditions, methamphetamine had a rate-increasing effect at doses that decreased VI rate. Results such as these have led to the conclusion that certain doses of amphetamine increase low rates of responding while decreasing high rates (see reviews by Grossman and Sclafani, 1971; Kelleher and Morse, 1968; Weiss and Laties, 1969). This conclusion is not supported by the present finding that there was no rate-increasing effect in the VI + signal or VT components at any dose of *d*-amphetamine (Figures 2, 3, and 4).

The failure of *d*-amphetamine to increase the low overall rate of responding in the VI + signal component is consistent with previous research. Carey and Kritkausky (1972) found that *d*-amphetamine (1 mg/kg) did not affect the response rate of rats under a differential-reinforcement-of-low-rate (DRL) schedule when reinforcement availability was signalled; the drug did increase DRL responding in the absence of signalled reinforcement. Laties and Weiss (1966) studied the effects of varying doses of *d*-amphetamine on the re-

sponding of pigeons under a fixed-interval (FI) schedule with an added "clock", where external stimuli varied systematically with time. Their results showed that the drug affected responding less under the FI clock condition, where the overall control rate was relatively low, than under a conventional FI schedule. Taken together, these results suggest that a low overall rate of responding under strong stimulus control will be relatively resistant to the rate-increasing effects of *d*-amphetamine. That *d*-amphetamine did not increase VT responding may be another example of the recognized insensitivity of very low rates of responding to the rate-increasing effects of this drug (see review by Kelleher and Morse, 1968; McMillan, 1968, 1969).

The failure of *d*-amphetamine to increase responding in either low-rate component raised the question of whether the low rates could be increased by any drug. To investigate this question, a single dose of phenobarbital (40 mg/kg) was administered. This drug and dose were selected on the basis of previous research in this laboratory (Thompson, 1972). The Thompson (1972) study showed that (1) phenobarbital could produce a large enhancement of progressive-ratio performance of pigeons by shortening post-reinforcement pausing and (2) the optimal dose for this effect was 40 mg/kg. The present finding that 40 mg/kg of phenobarbital increased response rate in both the VI + signal and VT components (Figures 2, 3, and 4) indicates that *d*-amphetamine's failure to do so was not the result of a general baseline insensitivity to all drugs. The present results also indicated that the rate-increasing effect of phenobarbital occurred only when the control rate was relatively low; when the control rate was higher (the VI component of both multiple schedules), the drug had a slight rate-decreasing effect (Figure 2). Similar rate-dependent drug effects have been found with other barbituates. In a study using pigeons under a *mult* VI VI + punishment schedule, Morse (1964) found that amobarbital (10 mg) increased response rate in the punished (low rate) component but decreased response rate in the nonpunished (high rate) component.

One aspect of the rate-decreasing effect of the largest dose of *d*-amphetamine (4 mg/kg) was surprising, namely, the complete suppression of responding in the signalled component of the *mult* VI VI + signal schedule (Figure 3). Although responding in the VI component was reduced by this dose, it was not completely suppressed. One interpretation of this selective suppression involves a re-definition of the VI + signal component. By experimenter definition, this is a single component. However, the pigeon's differential responding under control conditions suggests that two components were involved: (1) extinction in the absence of the signal and (2) continuous reinforcement or FR 1 in the presence of the signal. Because the probability of responding in the presence of the signal was relatively high under control conditions, the drug effect may simply be an example of amphetamine's well-known tendency to decrease high probability behavior. This redefinition of the VI + signal component can also be extended to explain the contrast effect that was found under *mult* VI VI + signal during baseline training (Figure 1). Many studies have shown that extinction in one component will increase VI responding in the other component of a multiple schedule (see reviews by Dunham, 1968; Freeman, 1971; Terrace, 1966).

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