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Verbal Responding Under a Fixed-Interval Schedule: Effects of D-Amphetamine[1]

MAXINE L. STITZER

Departments of Psychiatry D-5-West, The Jouns Hopkins University School of Medicine and Baltimore City Hospitals, Baltimore, MD 21224

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STITZER, M. L. *Verbal responding under a fixed-interval schedule: Effects of d-amphetamine.* PHARMACOL BIOCHEM BEHAV **21**(1) 67–72, 1984.—The purpose of this study was to characterize the effects of d-amphetamine (5–30 mg) on rate and distribution of verbal responding which was maintained under a fixed-interval (FI) schedule of reinforcement. Hired volunteer subjects simultaneously wrote and spoke narrative monologues; points were delivered under a multiple 5 min fixed-interval 1 min time out schedule for closure of a voice operated relay (VOR). Under placebo control conditions, most subjects paused for 2–4 minutes following the 1 min time out then spoke and wrote during later portions of the interval. d-Amphetamine increased both the number of words written and seconds of VOR closure in a dose-related manner. In subjects who showed typical FI response patterning, the drug generally decreased the length of early interval pausing and increased low control amounts of verbal responding which occurred early in the interval proportionately more than higher amounts of verbal responding seen during later portions of the interval. These drug effects on response patterning were generally similar to those seen in infrahuman species responding under fixed-interval schedules of reinforcement.

d-Amphetamine Response patterning Verbal behavior Rate-dependent drug effects Handwriting Subjective drug effects Fixed-interval schedules Human behavioral pharmacology

DRUGS generally have characteristic effects on operant performance which is maintained by schedules of reinforcement, effects which are related to on-going rates and patterns of responding. At moderate doses, several drugs typically increase low rates of responding while simultaneously decreasing or leaving unchanged higher rates of responding [4, 10, 12, 14]. Fixed-interval schedules have been used extensively to study these rate-dependent drug effects since this schedule of reinforcement typically generates a variety of local response rates which may be differentially changed by drug. Although the rate-dependent effects of drugs on operant performance under fixed-interval schedules have been thoroughly characterized in infrahuman species [4, 10, 12, 14], there is little information about drug effects on human fixed-interval performance. A recent study by Tewes and Fishman [16] examined the dose-effects of d-amphetamine and diazepam on high and low rates of lever pull responding which were generated in human subjects by delivering points under a fixed ratio or a fixed-interval schedule respectively (mult FR 30 FI 5 min schedule). In this study, effects of d-amphetamine were not similar to those typically seen in infrahuman species. In particular, d-amphetamine increased high rates of fixed ratio responding but did not increase lower rates of fixed-interval responding. Additional studies of drug effects on human schedule-controlled responding would be of interest because such studies can provide information about the cross species generality of behavioral drug effects.

Although arbitrary operant responses such as lever pulls are most similar to responses used in behavioral pharmacology studies with animals, there are other types of responses which might be used to study drug effects in humans. Previous studies have shown that drugs influence human talkativeness. In particular, d-amphetamine has been shown to increase human verbal output during dyadic social conversation [7,15], during isolated speech monologue production [6, 9, 15] and when narratives are handwritten [8]. In view of this sensitivity to rate-increasing effects of d-amphetamine, verbal responding may have utility for studying drug effects on schedule-controlled performance. If typical patterns of schedule-controlled verbal behavior could be generated by delivering reinforcement for verbal responding, then drug-produced changes in rates and patterns of responding could be examined to determine whether these are functionally similar to behavioral drug effects which have been observed when operant responding of infrahuman species is maintained under schedules of reinforcement.

The first objective of the present study was to determine whether typical patterns of pausing and responding could be developed when points were delivered under a fixed-interval schedule for verbal responding. The particular response used, simultaneous speaking and writing, was chosen because it incorporated both narrative speech which had been used in previous drug studies in this laboratory and handwriting which has been sensitive to schedule-control effects in previous studies [5]. Providing that typical patterns of

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schedule-controlled verbal behavior could be generated, the primary purpose of the present study was to characterize the effects of d-amphetamine on rates and distribution of responding within the fixed interval. In the present study, typical response patterning was generated in most subjects when reinforcement was delivered under a fixed-interval schedule for verbal responding. In these subjects, d-amphetamine changed rates and patterns of responding in ways which were generally similar to those seen in infrahuman species whose operant responding is maintained under fixed-interval schedules of reinforcement.

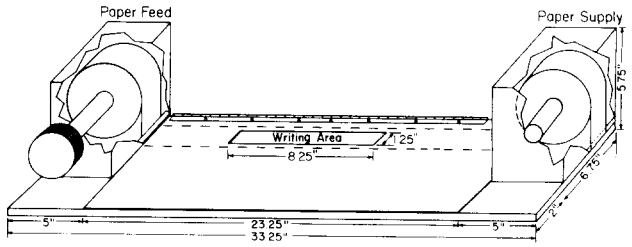


FIG. 1. Schematic diagram of the handwriting apparatus.

METHOD

Subjects

Five hired volunteers participated; four were female and one (DG) was male. All were between 19 and 21 years of age; body weights ranged from 48 to 91 kg (average=68 kg). Only one subject (CG) reported prior experience with drugs other than marihuana and alcohol. This subject had used stimulants, sedatives and LSD in the past. As far as current drug use was concerned, three subjects (PS, CG, BS) reported using marihuana once per week or more frequently and were regular cigarette smokers. All subjects reported at least occasional use of alcohol. All subjects passed medical and psychiatric screening and provided informed consent prior to participation.

Apparatus

During experimental sessions subjects were seated in a small room containing a desk, chair and array of stimulus lights on a panel above the desk. Subjects wore cushioned headsets with a low impedence boom microphone attached. Vocalization into the microphone activated a voice operated relay (VOR) with a brief attack time of about 0.6 sec and a longer release time of about 1.5 sec. VOR closure activated a feedback light located on the front panel as well as counters, timers and a cumulative recorder in the adjoining room. While the VOR remained closed, the counters and recorders advanced at a rate of once per second.

The apparatus used to collect handwriting data is shown in Fig. 1. It consisted of a flat board approximately 9×30 inches with a locked box mounted on each end. Inside each box was a horizontally mounted dowel. A roll of adding machine tape was held on the right-hand dowel, fed across the board and attached to the left hand dowel. The paper could be advanced across the board by turning a knob which protruded from the left hand box and rotated the dowel inside the box. The paper strip lay under a hinged metal plate which rested on top of the board between the paper feed boxes. A window approximately 1×8 inches in the center of the metal plate allowed access to the paper for writing.

Procedures

Prior to participation, subjects were told that they would be in an experiment in which drug effects on behavior would be studied, that they might receive a variety of medications including tranquilizers, sedatives and stimulants, and that their behavior would be observed and recorded during daily 2 hour sessions. To facilitate drug absorption, subjects were instructed not to eat for 2 hours before coming to the laboratory and were not allowed to eat while at the laboratory. To avoid drug interactions, subjects were instructed to abstain from any recreational drugs other than coffee or cigarettes for 12 hours prior to their laboratory appointments. During sessions, neither wristwatches nor personal items including cigarettes were allowed in the experimental room and subjects were instructed not to fall asleep.

Narrative speaking and writing was generated by instructions which were delivered both in a written notice and verbally by the experimenter. Subjects were told in the instructions that they should write during sessions and that they must read aloud anything that they wrote either while writing or immediately afterward. Subjects were told in the instructions that they could write about any topic they liked and that they could write as much or as little as they liked; alternative activities were reading a local daily newspaper provided or doing nothing. Subjects were told that they would earn points worth money by writing and talking but were not told what component of their behavior would result in point delivery.

Points worth 20 cents each were available under a fixed-interval (FI) 5 min schedule for closure of the VOR. Points were delivered by advancing a counter located on the front panel. A point was delivered if the VOR was already closed or for the first closure after each 5 min interval elapsed. Point deliveries were followed by a 1 min time out (TO) period during which stimulus light conditions changed; fixed intervals were timed from the offset of this time out period. Subjects were instructed to stop writing each time a point was earned, to draw a slash on the paper strip, turn to a fresh piece of paper and wait for the time out light to extinguish before beginning to write again. Sessions terminated following the first point delivery after 2 hr had elapsed from the session start; the maximum number of fixed-intervals possible during a session was 20, the minimum number earned was 16; 18–20 intervals were generally completed during a typical session.

During initial sessions, subjects BS and DW wrote continuously. In an attempt to suppress continuous writing, these subjects were told that they must copy everything they wrote below the original writing on the paper strip, but need only read what they wrote once. The additional handwriting requirement suppressed writing for subject BS and was kept in effect for the remainder of the experiment but the double writing requirement was withdrawn prior to active drug ingestion for subject DW when it failed to suppress her rate of writing.

One hour prior to each daily session, subjects orally ingested opaque capsules which contained placebo or active drug. Placebo only was given during the first 17–24 days while responding stabilized. Following this, active doses were administered under double blind conditions in mixed order with at least one placebo day intervening between

active doses. Placebo control data for each subject are based on 4–8 sessions interspersed throughout the study which were not preceded by an active drug day. Active doses were repeated 2 times for subject CG, 3 times for subjects BS and DW and 5–6 times for subjects PS and DG, with the number of replications for a given subject depending on the duration of their participation in the study. Subject PS received 5 and 15 mg of d-amphetamine. Subject CG received 10 and 20 mg, subject DW received 5, 10 and 20 mg while subjects DG and BW received 5, 20 and 30 mg d-amphetamine. The dose range for all subjects except PS was established on the basis of initial response to a 20 mg dose. If either behavioral or subjective measures revealed a typical stimulant drug effect, then the maximum dose was restricted to 20 mg.

Data Analysis

Four measures were used in data analysis: (1) words written; a technician blind to drug condition counted the total number of words written each day either directly from the paper strips or from typed transcripts. (2) Seconds of VOR closure; each VOR closure in excess of 1 second operated a counter, and once the relay was closed, the counter advanced once for each additional second of relay closure. VOR closure time was cumulated separately during each successive 30 sec time segment within the 5 min fixed interval. (3) Seconds of pre-response pausing; elapsed time between onset of the fixed interval component and the first VOR closure was cumulated; (4) total score on stimulant items of an adjective checklist. Immediately after each session, subjects completed a 48 item adjective checklist developed in this laboratory on which they rated the extent to which each item applied to their current mood on a scale of 0–3. Seventeen items were scored which have been previously enumerated and shown to be sensitive to d-amphetamine [7,15].

Because subjects did not all receive the same drug doses, statistical analysis was conducted using polynomial regression analysis [3] which evaluates the significance of linear trends in the dose-effect functions for individual subjects. Data were then examined for an overall group effect by determining the significance of the average z transformed correlation coefficient for the group. Significance levels were determined using the average number of observations (N=15) entered into individual subject correlations.

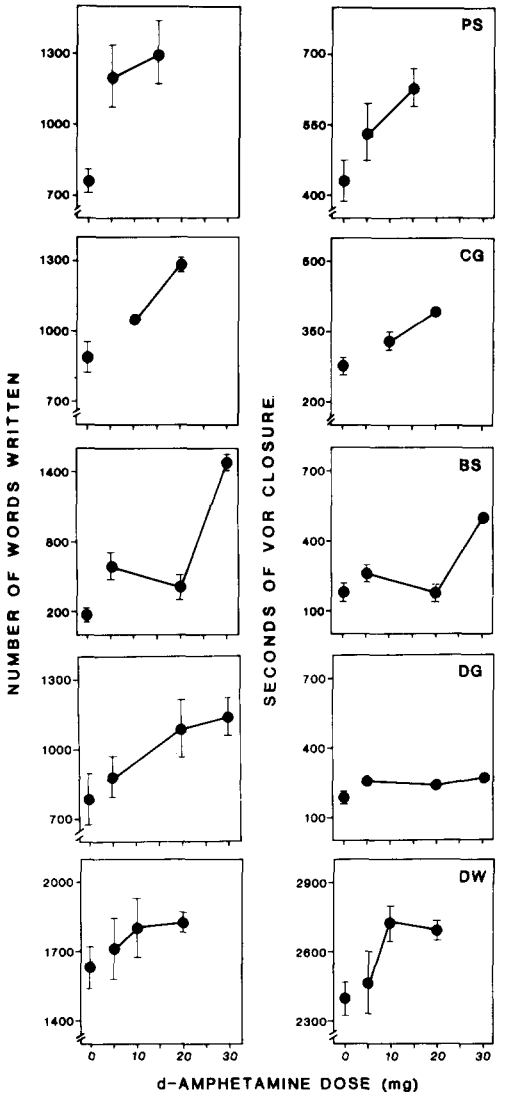


FIG. 2. Average number of words written (left-hand column) and average seconds of VOR closure (right-hand column) during a 2 hour session are shown for 5 individual subjects as a function of d-amphetamine dose. Data for active drug doses are based on 2 (CG), 3 (BS, DW) and 5–6 (PS, DG) observations. Brackets are ± 1 SEM.

RESULTS

Figure 2 shows total words written and total seconds of VOR closure for five study participants as a function of d-amphetamine dose, while results of the regression analysis on these data are shown in Table 1. Average number of words written during two hour placebo control sessions ranged from 189 for subject BS to 1637 for subject DW, while subjects PS, CG and DG wrote on the average 755, 883 and 788 words respectively after placebo. Total words written increased in a dose-related manner after d-amphetamine for all subjects. The average magnitude of increase in total words written at the highest dose administered to each subject was 238, 358, 397, 547 and 1308 words for subjects DW, DG, CG, PS and BS, respectively. Regression analysis was significant at $p<0.05$ or better for all subjects except DW and the average correlation for the group (r=.62) was significant at $p<0.02$.

As shown in the right-hand panel of Fig. 2, dose-related increases in total seconds of VOR closure were also observed following d-amphetamine ingestion. As shown in Table 1, regression analysis revealed significant ($p<0.05$ or better) dose-related effects for three subjects while for two subjects (DW, DG) regression coefficients did not quite reach accepted levels of significance. Average regression coefficient for the group (r=.61) was significant at $p<0.02$.

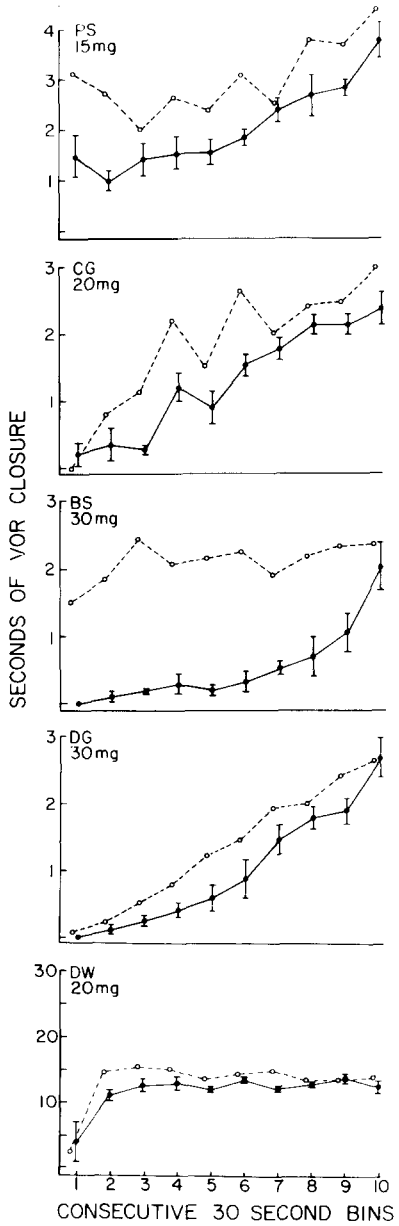
Correspondence between the amount spoken and amount written by each subject can be seen visually in Fig. 2, where similar dose-effect functions are generally apparent for the speaking and writing measures. The one exception was subject DG, whose dose-effect function for seconds of VOR closure appears flat compared to his function for words written. The correspondence between amount of speaking and amount of writing was further examined by calculating Spearman rank order correlations for each subject between

TABLE 1

REGRESSION ANALYSIS RESULTS

Subject	Words written r	Words written p	Seconds of VOR closure r	Seconds of VOR closure p	Seconds of pre-response pausing r	Seconds of pre-response pausing p	Adjective checklist r	Adjective checklist p
PS	.60	0.01	.57	0.02	−.61	0.01	.81	0.01
CG	.72	0.05	.79	0.01	−.68	0.05	.78	0.02
BS	.79	0.01	.65	0.02	−.68	0.01	.33	ns
DG	.49	0.05	.41	0.10	−.33	ns	.21	ns
DW	.41	ns	.56	0.10	.03	ns	.71	0.01
Average*	.62	0.02	.61	0.02	.49	0.10	.62	0.02

*After z transformation.



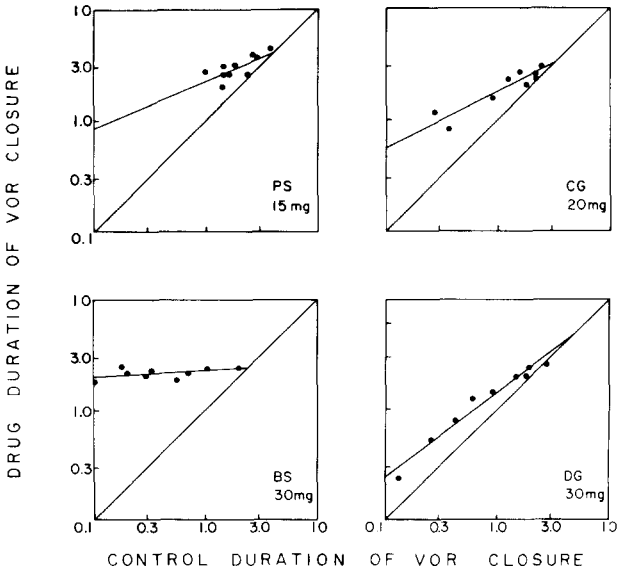


FIG. 4. Average duration of VOR closure (seconds) during each successive 30 sec segment of the 5 min fixed interval is graphed as a function of the average duration of VOR closure during that same 30 sec FI segment under placebo control conditions. Both scales are in log seconds. FI segments during which average control response duration was less than 0.1 sec have been excluded (subjects CG, BS, DG). The diagonal line represents no drug effect (drug duration of responding equal to control duration of responding). Regression lines have been fit to data points by the method of least squares.

FIGURE AT LEFT

FIG. 3. Average seconds of VOR closure are shown for individual subjects during successive 30 second segments of the 5 min fixed-interval. Data are shown separately for placebo control sessions (●—●) and for sessions following administration of the highest d-amphetamine dose studies in each subject (○— —○). Brackets around placebo control points are ±1 SEM.

words written and seconds of VOR closure during each experimental session. These correlations were .96, .95, .79, .71 and .67 for subjects CG, BS, DW, PS and DG respectively; all were significant at $p<0.01$.

Average duration of pre-response pausing within the fixed-intervals provided one measure of drug-produced shifts in patterns of verbal responding within the intervals. During placebo sessions, subjects paused on the average for 36 (DW), 127 (PS), 172 (CG), 209 (DG) and 245 (BS) seconds before the first VOR closure. d-Amphetamine produced dose-related decreases in pre-response pausing in three of five subjects (PS, CG, BS); linear regression coefficients were significant at $p<0.05$ or better for these subjects (Table 1) but the average coefficient for the group (r=.49) did not reach accepted levels of significance ($p<0.10$).

A second indication of drug-produced shifts in response patterning was obtained by examining the distribution of VOR closure time during successive 30 second segments of the fixed-interval. As shown in Fig. 3, after placebo four of the five subjects displayed gradually increasing amounts of vocal responding during successive 30 second periods of the fixed interval; the exception was subject DW who paused briefly at the start of each interval then wrote and spoke at a high terminal rate for the remainder of the interval. Figure 3 also reveals that d-amphetamine generally increased the amount of vocal responding during all segments of the fixed interval, except for responding during the first 30 second interval segment in subjects CG, DG and DW.

The relationship between response patterning during placebo control sessions and drug produced changes in response patterning is further examined in Fig. 4, which presents average seconds of VOR closure in each 30 second time period after the highest drug dose for that subject as a function of average seconds of VOR closure in that same time period during placebo control sessions. For subject BS (lower left panel) there was no relationship between control response patterning and drug produced changes in patterning: after 30 mg d-amphetamine this subject simply responded at a high steady rate throughout the fixed interval. For subjects PS, CG and DG, on the other hand, the magnitude of drug-produced increase in verbal responding during a given portion of the fixed interval was inversely related to the overall amount of control responding during that portion of the fixed interval. Specifically, shorter average durations of VOR closure which occurred early in the interval were increased by drug relatively more than longer average durations of VOR closure which occurred later in the intervals.

Three of five subjects (CG, PS, DW) showed orderly dose-related increases in adjective checklist scores and significant regression coefficients (Table 1). Subject CG had an average score of 8.8 after receiving placebo and an average score of 19.5 following 20 mg d-amphetamine. For subject PS average adjective checklist score was 18.0 after placebo and 46.7 after 15 mg d-amphetamine, while for subject DW the average score was 9.0 after placebo and 21.0 after 20 mg d-amphetamine. Two other subjects did not show dose-related increases in adjective checklist scores after d-amphetamine and had nonsignificant regression coefficients (Table 1). Average placebo control scores were 29.6 and 36.7 for subjects DG and BS respectively while average scores for these subjects following 30 mg d-amphetamine were 30.7 and 43.3. In spite of variability in individual subject response, the average regression coefficient for the group on the adjective checklist measure (r=.715) was significant at $p<0.01$).

DISCUSSION

In the present study, distribution of vocal responding during a mult FI 5 min TO 1 min schedule of point delivery was similar to the patterning obtained when infrahuman organisms emit operant responses under fixed interval schedules of reinforcement. Specifically, subjects paused for 2–4 min at the beginning of the 5 min interval and generally restricted their responding to later portions of the interval. When seconds of VOR closure were cumulated over the session within each 30 second interval segment, amount of vocal responding showed a gradual acceleration during successive interval segments (Fig. 3). As noted by Branch and Gollub [2], this composite pattern may be due in large part to the averaging of different length pauses at the start of each interval.

Although it has traditionally been difficult to generate typical fixed-interval response patterning with humans, there are several conditions which appear to facilitate such patterning. These include the use of high force response requirement [1, 11, 16] and presentation of the FI as part of a multiple schedule such as FI FR [5,16]. Response patterning obtained in the present study under a mult FI 5 min TO 1 min schedule with a combination writing and speaking response is consistent with the results of Gonzalez and Waller [5] who demonstrated typical FI response patterning when points were delivered under a mult FI 5 min FR 15 schedule for handwriting. Addition of the handwriting requirement may be critical for obtaining response patterning with a verbal response since in a previous study by Stitzer *et al.* [15] no patterning was seen when points were delivered under a FI 5 min schedule for VOR closure to subjects emitting narrative verbal monologues. The handwriting requirement may function in a similar fashion as a high response force requirement by counteracting the tendency of humans to respond at high steady rates in laboratory settings, a situation which precludes the development of patterning. Thus, the one subject in the present study (DW) who continued to respond at a high steady rate in spite of the handwriting requirement showed no acceleration of responding during the fixed interval. Other procedural differences including the length of the post-reinforcement time out may also have contributed to the differential success in obtaining schedule control in this study and the previous study which utilized only a spoken verbal response [15].

The present study has shown that d-amphetamine produces dose-related increases in human verbal behavior when subjects simultaneously write and speak narrative monologues. This extends previous observations that d-amphetamine increases human speech output during narrative monologue production which is either spoken [6, 9, 15] or written [8]. In the present study, drug-produced increases were apparent under conditions where sessions were quite lengthy (2 hr), where temporal response patterning developed under a schedule of point delivery and where subjects had an alternative response option, namely reading the newspaper. The one subject (DW) who failed to show a reliable increase in amount written after d-amphetamine had a very high baseline rate of writing output, which may have precluded observation of further increases.

Moderate doses of d-amphetamine typically have rate-dependent effects on operant responding of infrahuman species. That is, the drug increases low rates of responding while high baseline rates are increased less or may be decreased [2,13]. This rate-dependent relationship clearly

holds as well when local rates of responding within a fixed-interval schedule are examined. Since in the present study, most subjects paused at the beginning of the intervals and emitted their vocal responding during the later portions of the interval, a detailed analysis of drug effects on local response patterns during the interval could be made. This analysis revealed a general similarity between d-amphetamine effects in human and infrahuman species. Specifically, vocal responding generally began earlier in the interval after d-amphetamine than after placebo administration, and in three of four subjects increases in amount of vocalization tended to be proportionately larger early in the interval where control amounts of responding were relatively low than during later portions of the interval where control amounts of responding were higher (Figs. 3, 4). The failure of drug to increase responding during the first interval segment when control amounts of responding were zero is also consistent with reports from infrahuman species [14].

A recent study by Tewes and Fischman [16] examined effects of d-amphetamine (5–20 mg) on human operant responding maintained under a mult FI 5 min FR 30 schedule of point delivery. In this study, d-amphetamine increased high rates of FR responding but did not consistently increase much lower rates generated under the FI schedule. In contrast to results of the present study, the Tewes and Fischman study suggested that d-amphetamine does not have effects on schedule controlled human responding which are comparable to effects seen in infrahuman species. Many procedural differences exist between the two studies which could explain discrepant results including the type of response employed. It is possible that a verbal response is more sensitive to rate-increasing effects of d-amphetamine than is a manual operant response.

In previous studies of drug effects on social and verbal behavior, a close correspondence has generally been observed between behavioral and subjective report measures of drug effects [7,15]. That is, subjects who show increases in vocal responding after d-amphetamine also report typical stimulant effects of alertness and euphoria on subjective report measures. In the present study, two of the subjects who increased the number of words written after d-amphetamine (BS, DG) failed to show increases on the stimulant items of the adjective checklist employed to measure subjective drug effects. These two subjects were unusual, however, in having very high baseline scores on the stimulant items of the checklist. While this does not preclude a drug effect, it may militate against observing a drug effect on the subjective report measure.

This study has shown that d-amphetamine increases the amount of vocal responding observed in human subjects who are producing simultaneously written and spoken narrative monologues while points are delivered for vocalization under a mult FI 5 min TO 1 min schedule. Temporal distribution of speaking and writing during the fixed intervals was similar to that observed in infrahuman species; that is, subjects paused at the beginning of the interval and emitted most of their responding during the later portion of the interval. In subjects where this type of response patterning developed, d-amphetamine decreased the average length of early interval pausing and increased lower control amounts of responding which occurred early in the interval proportionately more than higher control amounts of responding which occurred late in the interval. These changes in response patterning are similar to drug effects which have been observed in infrahuman species emitting operant responses for food reinforcement under comparable schedules of reinforcement.

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