Pharmacology Biochemistry & Behavior, Vol. 9, pp. 57–63. Printed in the U.S.A.

Effects of d-Amphetamine on Speaking in Isolated Humans

MAXINE L. STITZER, ROLAND R. GRIFFITHS AND IRA LIEBSON

Department of Psychiatry, Baltimore City Hospitals
and
Department of Psychiatry and Behavioral Sciences
The Johns Hopkins University School of Medicine, Baltimore, MD 21205

(Received 8 December 1977)

STITZER, M. L., R. R. GRIFFITHS AND I. LIEBSON. *Effects of d-amphetamine on speaking in isolated humans.* PHARMACOL. BIOCHEM. BEHAV. 9(1) 57–63, 1978.—The effects of oral d-amphetamine, 5–20 mg were studied in isolated humans who produced speech monologues during experimental sessions. Drug effects were studied under double-blind conditions by making repeated observations within each subject after placebo or active drug. In the first experiment, d-amphetamine 15 mg was studied in 4 isolated subjects who had received instructions that they should talk some of the time during experimental sessions. All subjects spoke more after active drug than after placebo. In the second experiment, d-amphetamine 5–20 mg was studied in 4 subjects who were instructed to talk, but who also earned points under a fixed interval 5 min schedule by speaking (i.e. by closure of a voice operated relay). Point delivery did not generally influence patterns of speech over time. Reliable drug produced increases in amount of talking were observed in 3 of 4 subjects. Adjective checklist self report scores indicating a stimulant drug effect were also sensitive to effects of d-amphetamine. Under controlled laboratory conditions, an increase in speaking is a reliable behavioral effect of d-amphetamine in isolated humans producing speech monologues.

Speaking d-Amphetamine Humans Fixed interval schedule Instructions

AN INCREASE in talkativeness is purported in drug lore to be one of the effects of amphetamines on human behavior and studies using subjective report questionnaires have shown that people report feeling more friendly and talkative after ingesting these drugs [14]. There have been, however, few controlled observations of stimulant drug effects on human verbal behavior and there is little information about the conditions under which such effects occur. Griffiths, *et al.*, [4] recently showed that d-amphetamine (5–30 mg) dramatically increased verbal social interactions over control levels in members of dyadic social interaction pairs who received active drug. In addition, a few investigators have reported small increases in verbal output after ingestion of d-amphetamine in subjects engaged in written [5] or spoken [3,6] verbal monologues. Thus, there is reason to believe that verbal behavior is sensitive to effects of d-amphetamine, and that enhanced speech production may be apparent both in social interaction situations and in situations that do not involve social interaction.

The main purpose of the present experiments was to examine the effects of d-amphetamine on quantity of human verbal output in situations where individuals were engaged in speaking monologues rather than interacting socially. The experiments utilized within subject methodology to determine the magnitude and reliability of drug effects in individual humans. Drug effects on verbal responding were studied under two specific experimental conditions. In the first experiment, d-amphetamine was studied in human subjects who produced daily speech monologues after having received instructions to talk during experimental sessions but with no environmental feedback or consequences for talking. In a second experiment effects of d-amphetamine on speaking were studied in a situation where points were delivered under a fixed interval schedule as a consequence of speaking. The purpose of this experiment was to determine whether rates and patterns of speaking could be altered by environmental consequences for verbal responding and whether drug effects would also be apparent under these conditions.

GENERAL METHOD

Subjects. Participants were five normal volunteers with no history of drug abuse and three individuals with histories of ethanol abuse (DA, HU, SH). Volunteers were medically screened for any health problems prior to participation. Most of the participants reported no prior experience with stimulant drugs. Exceptions were KH, who had used prescribed anorectic compounds for weight reduction and AC and TE, who reported some recreational use of stimulants in the past.

[1]Supported by USPHS grants DA-01022 and MH-26812.
[2]Reprints may be obtained from Maxine Stitzer, Department of Psychiatry, Baltimore City Hospitals, D-5-West, 4940 Eastern Ave., Baltimore, MD 21224.

TABLE 1
SUBJECT CHARACTERISTICS

	Subject	Sex	Age (years)	Body Weight (kg)
Experiment 1				
	LS	F	26	77.3
	DA*	M	50	52.3
	HU*	M	52	60.0
	SH*	F	38	68.2
Experiment 2				
	AC	F	24	51.4
	KH	F	33	83.0
	SP	F	24	65.9
	TE	M	22	61.4

* These subjects had histories of ethanol abuse and ingested 125 mg (SH) or 250 mg (DA, HU) disulfiram daily.

Table 1 shows the sex, age and body weight of all participants.

Apparatus. Studies were conducted in a sound attenuated experimental chamber (1.33 × 1.21 × 2.13 m high) with programming and recording equipment located in an adjoining room. The chamber contained a chair, a desk, and was illuminated by overhead lighting. An array of stimulus lights and a counter were located on a panel above the desk top and a microphone was located on the desk. This microphone was used to tape record experimental sessions. In addition, for all the subjects in Experiment 1 a low impedence crystal boom microphone (3.8 cm in diameter) on a cushioned headset was positioned in front of the subject's mouth about 3 cm from the lips. Speaking into the microphone activated a voice operated relay (VOR) with an attack time of about 160 msec and a release time of about 1.5 sec. Closure of the VOR activated a feedback light located on the front panel of the chamber and also activated a counter and a standard cumulative recorder which were in an adjoining room. While the VOR remained closed, the counter and recorder advanced at a rate of one count per second.

Drugs. Before each daily session subjects, who were blind to drug condition, orally ingested three opaque size 0 capsules. These contained either placebo or 5, 10, 15 or 20 mg d-amphetamine sulfate. Nurses and research assistants, who were also blind to drug condition, monitored drug ingestion to ensure that subjects swallowed the capsules. One subject (AC) who had difficulty swallowing the capsules, received drug in elixer form (SKF: 1 mg d-amphetamine sulfate per ml; 10% ethanol) mixed with pineapple juice to make a total volume of 180 ml. Placebo drinks for this subject consisted of 15 ml of Muscatel wine (the main ingredient of the elixer base) plus pineapple juice to make a volume of 180 ml.

Subjects received placebo during the initial 9–34 sessions (median=13 sessions) while amount of talking stabilized from day to day. After this, active drug administration began. For subjects HU and LS in Experiment 1 and for all subjects in Experiment 2, active drug was administered once or occasionally twice a week, but never on consecutive days. Placebo was administered on days that active drug was not scheduled and at least one placebo session generally intervened between active drug treatments. Order of doses was mixed, except for subject SP who received the majority of 15 mg doses prior to receiving 20 mg doses. Subjects DA and SH in Experiment 1 were exposed to three conditions in mixed order: no drug treatment, placebo and active drug (d-amphetamine 5 or 15 mg). Active drug was never given more than once a week, and placebo or no treatment days generally intervened between active drug treatments.

Participants were instructed not to eat for 2 hr before ingesting experimental drugs and not to take any recreational drugs (other than cigarettes and coffee) for 12 hr prior. Experimental sessions, which were conducted 3 or 4 days a week, began 1.5 (subjects DA and HU in Experiment 1) or 2 hr after drug ingestion. Subject KH (Experiment 2) had a 3 hr drug pretreatment time since she reported experiencing onset of drug effects after leaving the hospital when drug pretreatment time was 2 hr. No attempt was made to control subjects' activity during this waiting time except that they could not eat or drink or leave the hospital floor. Subjects generally read, played pool or socialized with staff members.

Subjective reports. Immediately after each session participants individually completed a 48 item paper and pencil adjective checklist on which they rated the extent to which each item applied to their current mood on a scale of 0 (not at all), 1 (a little), 2 (quite a bit), and 3 (extremely). Scores were calculated by adding subject ratings on the following seventeen items: lively, vigorous, carefree, alert, friendly, cooperative, goodnatured, understanding, cheerful, active, full of pep, assertive, outgoing, talkative, confident, self-revealing, social. The first seven items are from the Vigor-Activity Scale of the Profile of Mood States [9].

Instructions. Prior to participation, subjects were told that they would be in an experiment where drug effects on behavior would be studied. They were told that their behavior would be observed and their talking would be monitored during sessions. Although instructions indicated that subjects should talk during these sessions (see Method for Experiments 1 and 2), they were not told what aspect of talking (i.e., amount, content, volume, etc.) was of interest to the investigators. Subjects were told that they could talk about any topic at all during sessions, but humming, singing vocal exercises and whistling were forbidden as were chanting mantras and counting numbers aloud.

Wrist watches, reading material and other personal items were not allowed in the experimental room. Subjects could not smoke cigarettes during sessions and were instructed not to fall asleep. Sessions were monitored occasionally to make sure subjects were following all instructions. Data were discarded for any days on which the subjects were observed to have fallen asleep.

Subjects were told that they might receive a variety of medications including tranquilizers, sedatives and stimulants. Subjects were told that they would be paid a salary of about $2.60/hr, part of which might be based on points earned during experimental sessions. Salaries were paid weekly.

EXPERIMENT 1: MONOLOGUE TALKING

Method. Four subjects (Table 1) participated in an experiment in which responding was generated by instructions to talk. Subject LS, who was exposed to experimental sessions which lasted 40 min, received the following instructions on the first day of participation: "When the green light comes on you may talk into the microphone, but you don't have to talk. You may talk about anything at all. You may talk as much or as little as you like, but you should say something

occasionally, just so we will know you are awake. The blue light means the machine is recording your speaking. This light should always be on whenever you are speaking. Extraneous noise also activates the light so you should be quiet and still when not speaking. The white light means the session is over. Please pay attention to the lights." Subjects DA, SH and HU, who were exposed to experimental sessions of 10, 30 and 60 min respectively, received these instructions: "You are supposed to talk sometimes. You don't have to talk for the whole session. You may just sit and think for part of the time. However, you should also talk part of the time. You may talk for the whole session if you have a lot to say. When talking, you must speak facing the microphone. What you say will be tape recorded. Are there any questions?"

A technician who was blind to drug conditions counted from tape recordings the total number of words spoken during each session. Data were discarded from the first 9 (LS), 14 (DA), 21 SH) and 34 (HU) sessions while amount of talking stabilized from day to day.

Results. As shown in Fig. 1, subjects who had received instructions that they should talk some but not all of the time emitted substantial amounts of monologue speech during daily experimental sessions. There were no consistent differences in rates of talking on no treatment and placebo days for subjects DA and SH. Average rates on days when placebo was administered were 13.5 words/min for subject HU; 22.3 words/min for subject SH; 31.6 words/min for subject LS and 46.4 words/min for subject DA. These rates do not reflect constant talking during the session. For the subject whose data was also collected with a voice operated relay (LS), the relay was closed on the average during 28% of the session on placebo days and during 72% of the session on days when 15 mg d-amphetamine had been administered. Figure 1 also shows that the number of words spoken increased on days when 15 mg d-amphetamine was administered compared to placebo days. This was a consistent effect which was observed in all four subjects.

Subjective report data were available only for subject LS, and these are shown in Fig. 1. Scores on the adjective checklist items increased after 15 mg d-amphetamine.

Figure 2 shows typical cumulative records from a placebo session (top panel) and a d-amphetamine session (lower panel) for subject LS. Although some talking generally occurred throughout placebo sessions, this subject tended to talk more at the beginning than during the middle and end of these sessions. After 15 mg d-amphetamine, the VOR was closed almost continuously. In the example shown, the VOR was closed during 95.4% of the session.

EXPERIMENT 2: MONOLOGUE TALKING WITH POINT DELIVERY ON A FIXED INTERVAL SCHEDULE

Method. Four normal volunteers (Table 1) participated in an experiment in which they could earn points by operating the VOR. Points worth 20 cents apiece were delivered if the VOR was closed at the end of 5 min or for the first VOR closure after 5 min had elapsed. Point delivery was accompanied by a brief tone into the headsets worn by subjects. A green light on the front panel of the chamber was illuminated at the beginning of the session and extinguished at the end. Point delivery was followed by a 10 sec time out signaled by a red light. Sessions terminated following the first point delivery which occurred after 40 min had elapsed. Therefore there were a maximum of eight opportunities for point delivery during each daily session. Subjects received the following instructions on their first day of participation: "Your job is to talk and you get points for talking. You should try to earn as many points as possible as the points are worth money. You should talk only when the green light is on. No talking is allowed when the red light is on. You do not have to talk all the time to earn the maximum number of points.

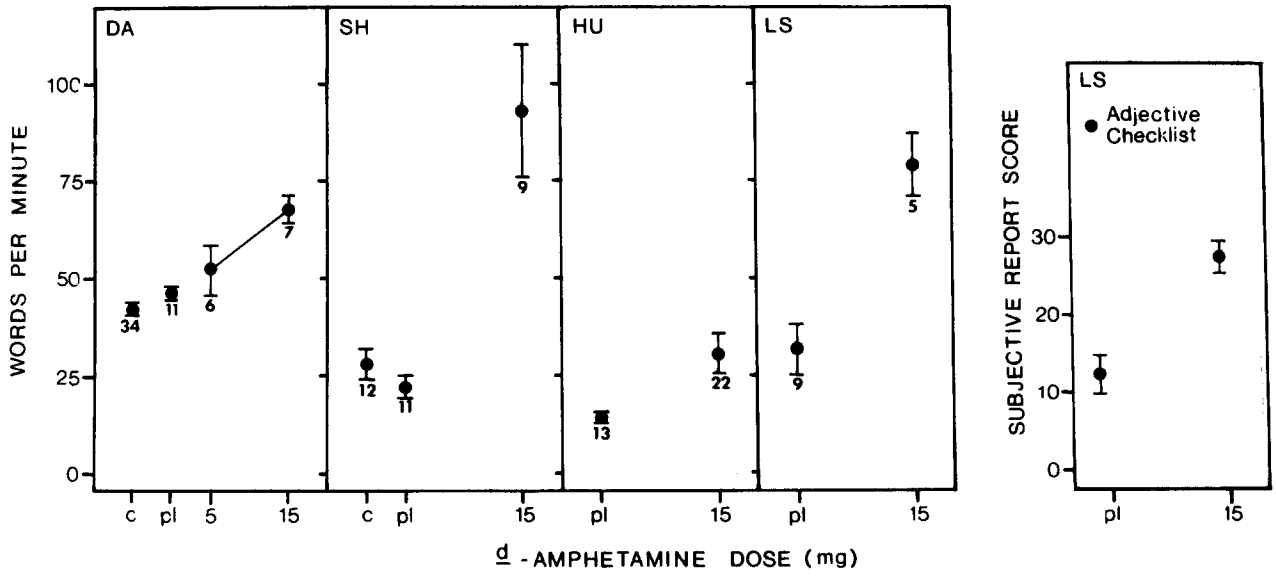

FIG. 1. Effects of placebo and d-amphetamine 5–15 mg on monologue talking in four individual subjects. Verbal responding is presented as average words spoken per minute. Points labeled C for subjects DA and SH are the mean of control (no drug) observations, while P1 indicates the mean at placebo observations. Brackets represent ±1 standard error of the mean. Number of observations are shown under each data point. Effects of placebo and d-amphetamine 15 mg on subjective report scores for subject LS are shown in the far right-hand graph. (See Method for description of subjective report measures.) Experimental sessions were 10 min for subject DA, 30 min for subject SH, 40 min for subject LS and 60 min for subject HU.

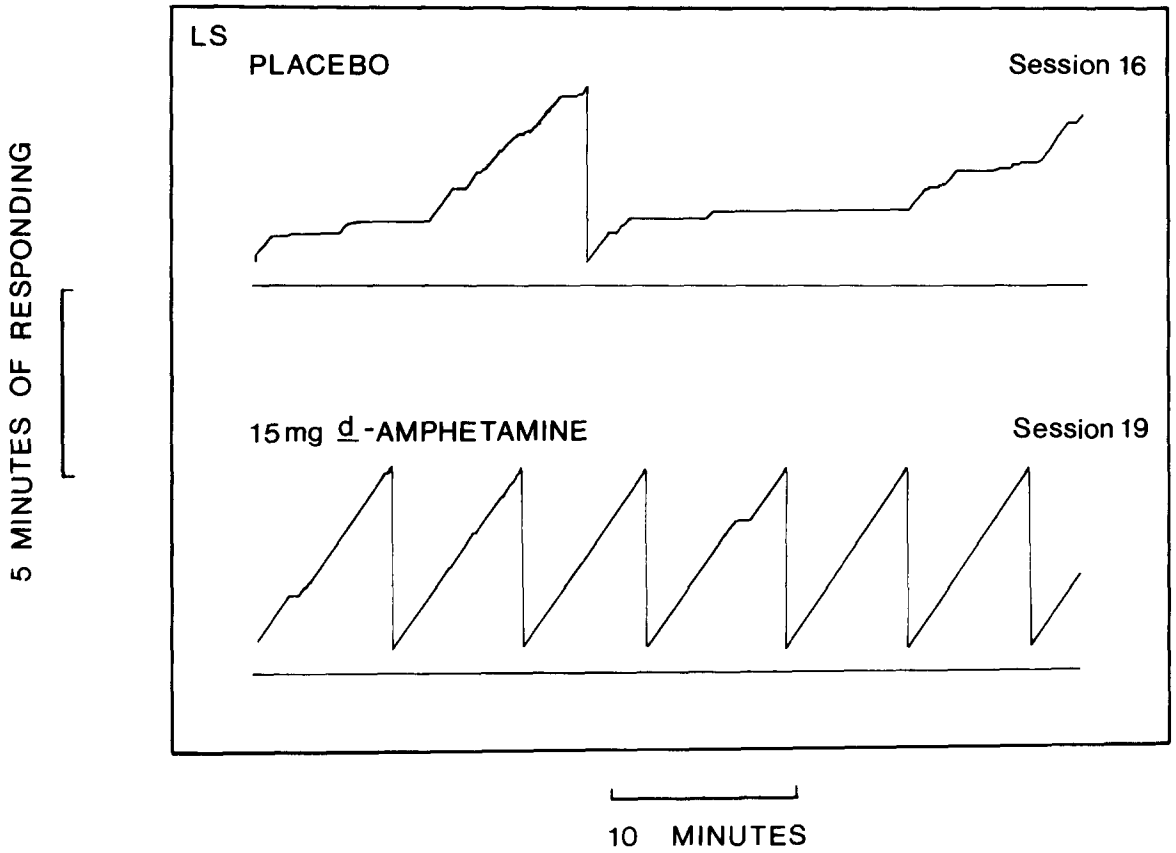

FIG. 2. Representative cumulative recordings of monologue speaking performance for subject LS after placebo (top) and d-amphetamine 15 mg (bottom). The response pen stepped once per second whenever a voice operated relay was closed. Entire 40 min sessions are shown.

When the green light is on you may talk but you do not have to talk. The blue light means the machine is recording your speaking. This light should always be on whenever you are speaking. Extraneous noise also activates the light so you should be quiet and still when not speaking. The white light means the session is over. Please pay attention to the lights."

Total time that the VOR remained closed was cumulated on a counter in an adjoining room and provided the quantitative measure used to evaluate effects of d-amphetamine on verbal responding. In order to study the distribution of speaking during the intervals, the 5 min interval was divided into 10 segments of 30 sec each and duration of VOR closure was cumulated for each segment over the entire session. Sessions were also tape recorded occasionally for subjects AC, KH and SP. A research assistant, blind to drug conditions, counted the number of words spoken during 10 one minute time samples spaced at irregular intervals throughout these sessions.

Data were discarded from the first 5 sessions of participation for subject TE while control responding stabilized; the first 21 sessions were discarded for subject SP due to a shift (decrease) in amount of control responding after drug administration initially began; the first 24 sessions were discarded for subject AC since she switched from capsules to an elixir form of medication and the first 57 sessions were discarded for subject KH during which she had received d-amphetamine with a two hr pretreatment time which was subsequently found to be too short.

Results. Subjects spent substantial amounts of time talking during experimental sessions. As shown in Fig. 3, talking occupied 36.4% of the session for subject AC on the average placebo day; 43.8% of the session for subject SP; 45% for subject KH and 80.8% for subject TE. Occasional word counts indicated that these percentage measures represented overall rates of about 50–100 words/min for subjects AC, SP and KH. Word counts are not available for subject TE who had an even higher rate of talking.

Patterns of responding during the 5 min interval were analyzed with a quarter-life measure. Quarter-life refers to the average proportion of the interval which has elapsed when one-quarter of the average total responses during the interval have been emitted [1]. A quarter-life of 0.25 indicates uniform distribution of responding throughout the interval while values higher than this indicate that responding is distributed in later portions of the interval. For three of the four subjects there was no particular pattern in the distribution of talking during the interval (quarter-life values of 0.3 or less), while one subject, KH, generally paused after point delivery and distributed her talking primarily in the later portions of the intervals. Average quarter-life during the last five placebo sessions for this subject was 0.53.

Figure 3 shows that three of four subjects talked more on days when they received d-amphetamine than on days when

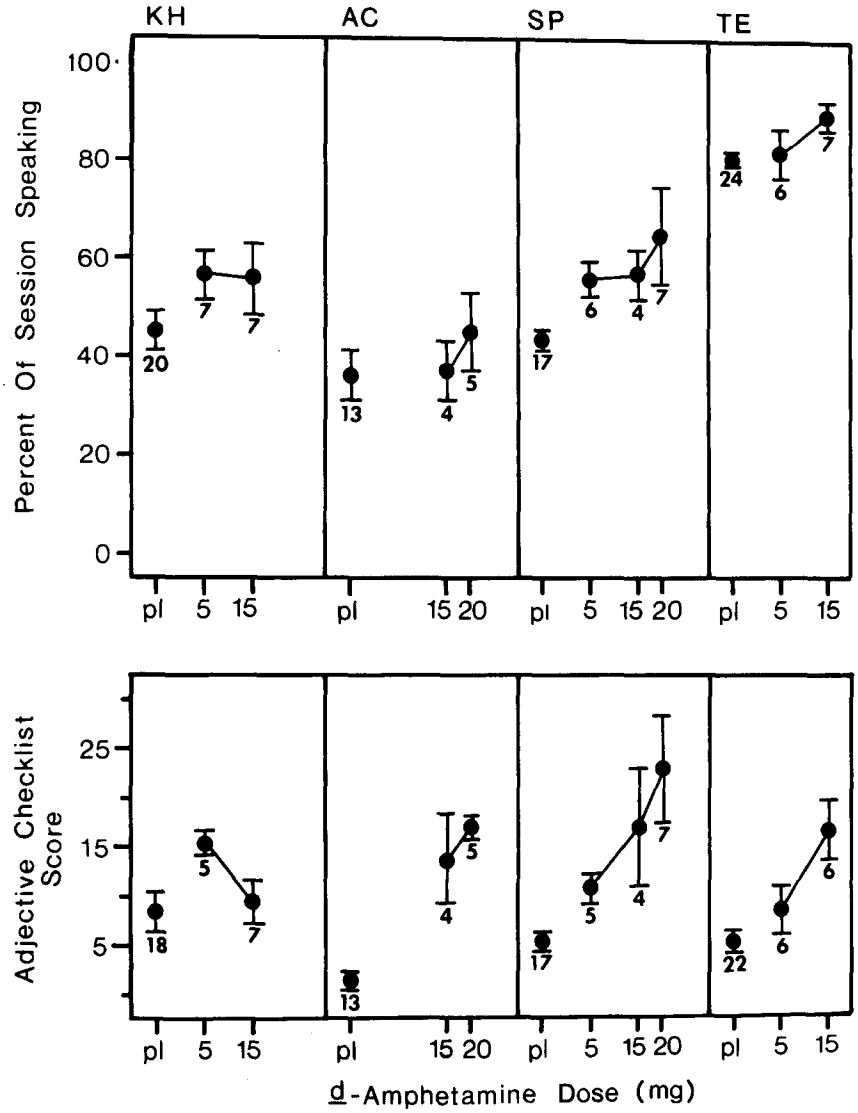

FIG. 3. Average effects of placebo (pl) and d-amphetamine 5–20 mg on monologue talking under a fixed-interval 5 min schedule of point-delivery (top) and on average score for 17 items of a mood adjective checklist (bottom) in four subjects. Percent of session speaking (ordinate) refers to percent of the session during which a voice operated relay was closed. Brackets are ±1 standard error of the mean. Number of observations are shown under each data point.

they received placebo, subject AC being the exception. The effect of d-amphetamine was generally dose related, although in two subjects (KH and SP) the 5 mg dose was behaviorally active and there was little difference between the average effects of 5 mg and 15 mg. The effect of d-amphetamine on talking is apparent for subject TE at the 15 mg dose in spite of his extremely high level of speaking during placebo sessions.

Figure 3 (bottom) shows an orderly dose related increase for 3 of 4 subjects (AC, SP, TE) in adjective checklist scores for items which indicate a stimulant drug effect, while subject KH shows an elevated adjective checklist score only for the 5 mg dose of d-amphetamine.

Cumulative records presented in Fig. 4 show selected examples of placebo performance (left-hand column) and performance after d-amphetamine (right-hand column) in individual subjects. Although there was considerable variability in the magnitude of the drug effect across observations for each subject, the increase in talking under d-amphetamine was very dramatic at times in all subjects.

DISCUSSION

Previous reports have shown slight or equivocal enhancement of verbal output by d-amphetamine. Gottschalk, *et al.* [3] for example, obtained short speech samples from 30 prison inmates before and after they ingested either placebo or 15 mg d-amphetamine. The average number of words spoken by the d-amphetamine group was slightly greater than that observed for the placebo group at 2

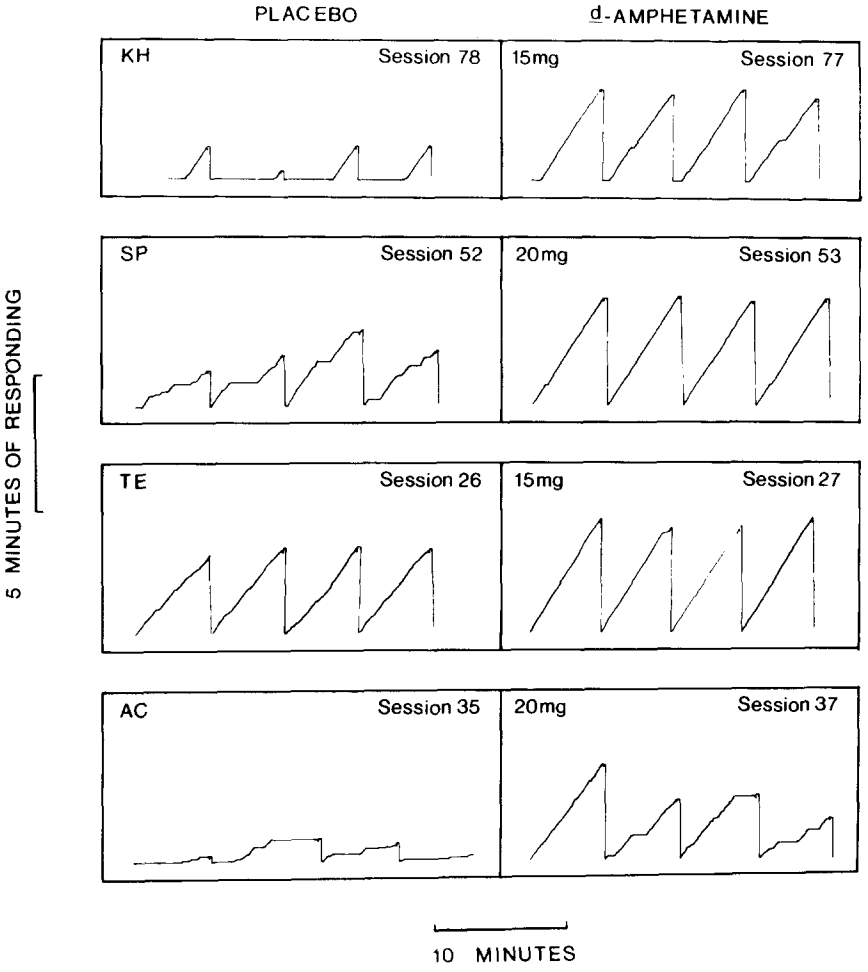

FIG. 4. Representative cumulative records of monologue talking with points delivered under a fixed-interval 5 min schedule. Examples of performance are shown for subjects after placebo (left-hand column) and after 15 or 20 mg d-amphetamine (right-hand column). The response pen stepped once per sec whenever a voice operated relay was closed, and reset after each reinforcer delivery. Portions of cumulative records shown are intervals 3 through 6 of the indicated sessions.

hr but not at 4 hr post ingestion. Similarly, Hurst [5] asked 72 college students to write for 20 min on an assigned topic at 2 hr and 50 min after ingesting placebo or d-amphetamine (14 mg/70 kg). Average verbal production increased 19% over placebo levels when subjects ingested active drug.

By using repeated observations methodology and individual subject analysis, the present study has extended these previous observations in several important ways. The facilitating effect of d-amphetamine on verbal output was shown to be dose related within individual subjects and the magnitude of the effect was quite substantial at higher doses. Facilitation of speech output was reliable and replicable in the same subjects and occurred when monologue speaking sessions varied from 10 min to one hr in length. Facilitation of speaking was observed in subjects who had widely different characteristic control rates of verbal output. Finally, facilitation of verbal output was observed in two rather different experimental situations: In Experiment 1, where speech monologues were generated only by instructions to talk, and in Experiment 2, where talking generated by instructions also resulted in point delivery under a fixed interval schedule.

In a previous experiment [4] d-amphetamine increased talking in the members of a social dyad who received active drug. The present experiments have shown that enhanced speech production after d-amphetamine does not require a social interaction situation, but is also observed with isolated subjects who are engaged in speech monologues. Thus an increase in the quantity of verbal behavior in humans appears to be a reliable behavioral effect of d-amphetamine both in social interaction and nonsocial situations.

In Experiment 2 an attempt was made to influence rates and patterns of human monologue speech generated with instructions by delivering points contingent on closure of a VOR under a fixed interval schedule. Overall rates of talking were substantially higher for subjects in Experiment 2 who could earn points for talking (50 words/min or higher) than for subjects in Experiment 1 who were simply instructed to

talk (13.5–46.4 words/min). An influence of point delivery on response patterning was less evident. In 3 of 4 subjects, no clear influence of point delivery on distribution of talking during the fixed intervals was observed. Previous research has demonstrated that written verbal behavior (handwriting) can be maintained by point delivery under a fixed interval schedule and that response patterning typical of FI schedule control develops [2]. The present study, however, did not explore conditions necessary for development of schedule control over monologue speech.

There is ample evidence that human subjects can reliably report a cluster of symptoms associated with ingestion of stimulant drugs on adjective checklist [11], and on questionnaire scales of the Addiction Research Center Inventory [7,8]. Similarly, adjective checklist scores were systematically related to drug ingestion and to drug dose in the present studies. The effects of d-amphetamine on the behavioral and subjective measures generally corresponded well within subjects. Thus, for example, both subjects who showed an elevated talking rate under 5 mg d-amphetamine (KH, SP) in Experiment 2, also reported a subjective drug effect at this dose. Some individual differences in response to d-amphetamine were noted in the present study. Subject KH (Fig. 3), for example, showed an increase in adjective checklist items indicating tension and anxiety rather than euphoria at d-amphetamine doses above 5 mg. Subject AC (Fig. 3) showed a dramatic increase on the adjective checklist score but little or no drug effect on the behavioral measure. Such individual differences in subjective and behavioral effects of d-amphetamine have also been noted by others [4, 10, 12]. On the whole, however, subjective report questionnaires and behavioral measures were equally sensitive to effects of d-amphetamine in individual subjects.

A speaking response has several unique advantages for studies of behavioral drug effects in humans. Speaking is a pervasive and important part of the human behavioral repertoire and as such may reflect significant aspects of behavioral drug effects. Speech in both isolated and socially interacting individuals [4] is quite sensitive to rate enhancing effects of d-amphetamine. This makes speaking somewhat unique since performance of humans on many motor and cognitive tasks is relatively insensitive to amphetamines under normal nonfatigued performance conditions [14]. Finally, although quantitative aspects of speech were emphasized in the present studies, verbal behavior provides a variety of both quantitative and qualitative experimental endpoints for analysis of drug effects (see [13]). The verbal response thus appears to be a promising candidate for future studies of behavioral drug effects in humans.

REFERENCES

1. Gollub, L. R. The relations among measures of performance on FI schedules. *J. exp. Analysis Behav.* **2:** 337–343, 1964.
2. Gonzalez, F. A. and M. B. Waller. Handwriting as an operant. *J. exp. Analysis Behav.* **21:** 165–175, 1974.
3. Gottschalk, L. A., D. E. Bates, I. E. Waskow, M. M. Katz and J. Olsson. Effects of amphetamine or chlorpromazine on achievement striving scores derived from content analysis of speech. *Comprehensive Psychiat.* **12:** 430–436, 1971.
4. Griffiths, R. R., M. Stitzer, H. Corker, G. Bigelow and I. Liebson. Drug produced changes in human social behavior: Facilitation by *d*-amphetamine. *Pharmac. Biochem. Behav.* **7:** 365–372, 1977.
5. Hurst, P. M., R. Radlow, N. C. Chubb and S. H. Bagley. Effects of alcohol and *d*-amphetamine upon mood and volition. *Psychol. Rep.* **24:** 975–987, 1969.
6. Jaffe, J., C. C. Dahlberg, J. Luria, S. Breskin, J. Chorosh and E. Lorick. Speech rhythms in patient monologues: The influence of LSD-25 and dextroamphetamine. *Biol. Psychiat.* **4:** 243–246, 1972.
7. Jasinski, D. R., J. G. Nutt and J. D. Griffith. Effects of diethyproprion and *d*-amphetamine after subcutaneous and oral administration. *Clin. pharmac. Ther.* **16:** 645–652, 1974.
8. Martin, W. R., J. W. Sloan, J. D. Sapira and D. R. Jasinski. Physiologic, subjective and behavioral effects of amphetamine, methamphetamine, ephedrine, phenmetrazine and methylphenidate in man. *Clin. pharmac. Ther.* **12:** 245–258, 1971.
9. McNair, D. M. and M. Lorr. An analysis of mood in neurotics. *J. Abnorm. Soc. Psychol.* **69:** 620–627, 1964.
10. Morselli, P. L., G. F. Placidi, C. Maggini, R. Gemeni, M. Guazelli, G. DeLisio, S. Standen and G. Tognoni. An integrated approach for the evaluation of psychotropic drugs in man. *Psychopharmacologia* **46:** 211–217, 1976.
11. Nowlis, V. and H. H. Nowlis. The description and analysis of mood. *Ann. N.Y. Acad. Sci.* **65:** 345–355, 1956.
12. Tecce, J. J. and J. O. Cole. Amphetamine effects in man: paradoxical drowsiness and lowered electrical brain activity (CNV). *Science* **185:** 451–453, 1974.
13. Waskow, I. E. The effects of drugs on speech: A review. In: *Research in Verbal Behavior and some Neurophysiological Implications,* edited by K. Salzinger and S. Salzinger. New York: Academic Press, 1967.
14. Weiss, B. and V. G. Laties. Enhancement of human performance by caffeine and the amphetamines. *Pharmac. Rev.* **14:** 1–36, 1962.