*EFFECTS OF d-AMPHETAMINE, CHLORPROMAZINE,
AND CHLORDIAZEPOXIDE ON INTERCURRENT
BEHAVIOR DURING SPACED-RESPONDING SCHEDULES¹*

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Effects of *d*-amphetamine, chlorpromazine, and chlordiazepoxide on lever pressing under direct control of spaced-responding schedules were compared with effects on intercurrent drinking and wheel running in the rat. Drug effects on lever pressing were systematically related to dose and were consistent for all animals; drug effects on intercurrent behavior were generally different for each animal. In the case of lever presses, increasing doses of *d*-amphetamine first increased and then decreased response rate, increasing doses of chlorpromazine produced graded decreases in response rate, and doses of chlordiazepoxide up to 40 mg/kg produced no effect on response rate. These data are discussed in context with the concept of schedule control, and it is suggested that the behavioral pharmacology of intercurrent behavior be explored as a useful procedure in the experimental analysis of intercurrent behavior.

Key words: intercurrent behavior, spaced-responding schedules, schedule control, *d*-amphetamine, chlorpromazine, chlordiazepoxide, rats

The concept of the "operant" was first formulated by Skinner (1938, p. 19), was reviewed by Catania (1974), and is recognized as a basic concept in the experimental analysis of behavior. The concept of "schedule control" was developed by Ferster and Skinner (1957), was discussed by Morse and Kelleher (1970), and is generally recognized as a basic concept in behavioral pharmacology (Dews, 1958; Kelleher and Morse, 1968).

Historically, the concept of schedule control has referred to characteristic, reproducible patterns of responding that occur when responses have scheduled consequences. Recently, however, there has been a renewed interest in the observation that characteristic, reproducible

patterns of behavior can also occur in the absence of scheduled consequences of specific responses. For example, under certain conditions, drinking reliably follows food ingestion in the absence of any scheduled relation between drinking and food presentation (*e.g.*, Falk, 1961). Similarly, wheel running (Levitsky and Collier, 1968; Skinner and Morse, 1957), air licking (Mendelson and Chillag, 1970), pica (Villarreal, 1967) and bar biting (Hutchinson, Azrin, and Hunt, 1968) have been reported to occur at specific times with respect to presentation of environmental stimuli not dependent upon occurrences of the response. This class of behavior, which is, in some sense, induced by the occurrence of certain environmental events and modulated by the schedule of presentation of those events, has been called "adjunctive behavior" (Falk, 1972).

A great deal is known about the behavioral effects of drugs on schedule-controlled operant behavior (*cf.* Kelleher and Morse, 1968). Less is known about the behavioral effects of drugs on so-called adjunctive behavior. There is evidence that dose-effect relations for amphetamine are different for schedule-controlled drinking and adjunctive drinking (Falk, 1969; McKearney, 1973; Wuttke, 1970). There is also evidence that comparative drug effects on

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schedule-controlled lever pressing and adjunctive drinking are different for amphetamine and chlorpromazine (Byrd, 1973, 1974). There is little information, however, concerning relations between rate and pattern of adjunctive behavior and drug effects. In most cases, drinking occurs at a uniformly high rate, and a very fine analysis of drug effects is needed to detect momentary rate changes (e.g., Knowler and Ukena, 1973). The effects of drugs on other adjunctive responses and across a wider range of response rates are not well explored.

The present experiments compared effects of *d*-amphetamine, chlorpromazine, and chlor-diazepoxide on rate of three responses. Because the terms "operant" and "adjunctive" describe classes of behavior whose members are determined empirically, other words should identify individual responses before they are classified. A simple specificity of individual responses in the present experiment is that occurrences of a lever press were directly related to the delivery of food under a spaced-responding schedule; occurrences of a wheel turn or lick on a water tube were not. An appropriate short-hand term to identify these latter responses is "intercurrent behavior". The term is descriptive with respect to the schedule of food delivery and does not prejudice subsequent assignment to a particular response class.

Previous experiments have indicated that a spaced-responding (or differential-reinforcement-of-low-rate) schedule of reinforced lever presses can generate characteristic patterns of intercurrent behavior (Laties, Weiss, Clark, and Reynolds, 1965; Segal and Holloway, 1963; Smith and Clark, 1974; Wilson and Keller, 1953). By comparing drug effects on schedule-controlled behavior and intercurrent behavior, the present experiments sought to extend observations of comparative drug effects on schedule-controlled and intercurrent behavior and to explore conditions under which behavioral pharmacology may contribute to the identification and experimental analysis of adjunctive behavior.

METHOD

Subjects

Three male Wistar rats (R1, R2, R3) were housed individually and maintained at approximately 80% of initially determined free-

feeding weights for the duration of all experiments. The rats were about six months old at the start of drug experiments and had been trained according to the procedure outlined below.

Apparatus

Experiments were conducted in cages mounted in ventilated, sound-isolated chambers. The experimental chambers have been described in detail by Smith and Clark (1974). Briefly, each cage consisted of a bidirectional running wheel with a Lehigh Valley rat lever, a food cup, and a water tube mounted on one wall. The water tube was connected to a Grason-Stadler Drinkometer Type E4690A. A running response was defined by the closure of a precision switch by either of two cams arranged 180 degrees apart on the running-wheel shaft. Movement of the running wheel required a tangential force of approximately 0.15 N. Each effective lever press required a force of 0.15 N and produced an audible click from a relay mounted behind the lever. Standard Noyes food pellets (0.045 g) were delivered by a Foringer feeder. Two 3-W incandescent lamps indirectly illuminated the experimental chamber at all times during the experimental session. Scheduling and recording equipment were located in an adjoining room.

Procedure

Before administration of drugs, all animals had been trained approximately 60 days under a multiple schedule containing three parameter values of a spaced-responding schedule, under which a minimum time between lever presses (interresponse time or IRT) was required for food presentation. Each parameter value was associated with the presence of a distinctive auditory stimulus (S^D). In the presence of a tone, the schedule parameter was 10 sec; in the presence of a clicking sound, the schedule parameter was 20 sec; in the presence of white noise, the schedule parameter was 60 sec. Lever presses in the absence of any scheduled auditory stimuli (S^A) never produced food pellets; S^D duration was 15 min and S^A duration was 5 min. Schedule parameter values occurred in a mixed order, each value occurring three times per daily 3-hr session. S^A periods occurred after each S^D period. Animals could turn the running wheel or lick the water

tube at any time, but these responses had no programmed relation with the schedule of food presentation.

Three drugs were studied under this procedure in the following order: *d*-amphetamine sulfate (0.3 to 4.0 mg/kg), chlorpromazine hydrochloride (0.25 to 2.0 mg/kg), and chlordiazepoxide hydrochloride (2.5 to 40.0 mg/kg). *d*-Amphetamine and chlorpromazine were dissolved in 0.9% NaCl solution. Chlordiazepoxide was dissolved in a commercial "Librium" solvent. Doses of drugs are presented in terms of salts. The volume of each dose was 1 ml/kg body weight and was injected into hind-leg thigh muscles twice a week at most. Drug effects were determined from single injections at each dose, and doses of each drug were studied in a mixed order. *d*-Amphetamine was injected 10 min before a session began; chlorpromazine and chlordiazepoxide were injected 30 min before the session. Saline injections were given 10 min before the session. After all injections, an animal was returned to its home cage during the prescribed delay period.

Lever presses, licks, running-wheel switch closures, and food delivery within each schedule component were recorded on digital counters and on separate channels of a strip chart recorder. In addition, lever presses and wheel-switch closures were recorded on separate cumulative recorders.

RESULTS

Rates and patterns of lever-press responses and rates of food delivery before drug experiments were similar to those reported both where IRT parameter was varied sequentially (Wilson and Keller, 1953) and where the parameter differed among multiple-schedule components (Zimmerman and Schuster, 1962). In general, lever-press rate, food frequency, and lick rate were all a decreasing function of increasing schedule parameter. Rate of wheel running was a different function of IRT value in different subjects, although running rate was generally higher at longer parameter values. A detailed discussion of response rates and response sequences before drug administration appears elsewhere (Smith and Clark, 1974).

Effects of d-amphetamine. The effects of *d*-amphetamine on response rate are shown in Figure 1. Each frame in Figure 1 shows drug

effects for a particular response (columns) at a particular schedule parameter value (rows) for all subjects. Points for lever pressing and running are based on responding during the first 2 hr of the 3-hr session in order to assess maximum drug effects. Points for licking are based on responding over the entire session. This difference in time sample for data points did not compromise general findings. Vertical lines about unconnected points indicate the range of response rates for five saline-control sessions.

Rate of lever pressing (left column) first increased and then decreased as dose of *d*-amphetamine increased, and rate of licking (center column) decreased as dose increased. There were no differences in these effects, which were systematically related to IRT value; the only exception to the general effects was a greater enhancement of lever-press rate for Rat 1. In contrast to consistent drug effects on rate of lever pressing and rate of licking, dose-effect curves for rate of wheel running (right column) were more varied between animals. Some of the general drug effects appeared to be related to control rate of running,

Fig. 1. Effects of *d*-amphetamine on mean rate of lever pressing (left column), licking (center column), and running (right column) at each schedule parameter (rows). Circles show effects for Rat 1; triangles, for Rat 2; squares, for Rat 3. Unconnected points with vertical lines indicate the mean and range of five saline control sessions.

Fig. 2. Effects of *d*-amphetamine on first-order conditional probability of selected response sequences under each schedule parameter for individual rats. Response sequences are lever following lever (Lv/Lv), run following lever (Rn/Lv), lick following lever (Lk/Lv), lever following run (Lv/Rn), run following run (Rn/Rn), lick following run (Lk/Rn), lever following reinforcement (Lv/Rft), run following reinforcement (Rn/Rft), and lick following reinforcement (Lk/Rft). Points at S are mean values for the first 2 hr of five saline control sessions; data points are mean values for the first 2 hr after a single injection of each dose. Points missing at larger doses are due to the elimination of the first response in a sequence.

with several exceptions. Thus, *d*-amphetamine, which produced characteristically different, yet consistent effects on rate of reinforced lever pressing and on rate of intercurrent licking, produced more variable effects on rate of intercurrent wheel running.

Figure 2 shows the effects of *d*-amphetamine on selected first-order conditional probabilities among different responses and for the response following food delivery. A previous experiment showed response sequences that included intercurrent responses to be systematically related to IRT parameter across animals when rate of intercurrent responding was not (Smith and Clark, 1974). Thus, the structure of response sequences may be an orderly function of certain variables when frequency of each response is not. It was of interest, therefore, to see whether or not changes in certain response sequences were an orderly function of *d*-amphetamine dose across animals when changes in intercurrent response rate were not and, in addition, to note whether drug effects on response sequence suggested a source of variability for the drug effects on intercurrent response rate. Computation formulae for the conditional probabilities appear elsewhere (Smith and Clark, 1974).

In general, Figure 2 shows that response sequences that included both a lever press and a run were more affected by drug doses than were response sequences that included a lick, and that the sequence of a response following food delivery was completely changed at larger doses for two rats. In addition, reference to Figure 1 shows that, in most cases, the relationship between the sequence "lever following lever" (Lv/Lv) and drug dose was similar to the relationship between lever-press rate and drug dose. Comparison of Figures 1 and 2 also shows that, in most cases, differences in dose effects on running rate were correlated with differences in effects on the response sequence "run following run" (Rn/Rn). Thus, without excessive attention to detail, it appears that while effects of *d*-amphetamine on rate of lever pressing and

Fig. 3. Effects of chlorpromazine on mean rate of each response. Points are arranged as in Figure 1.

wheel running were associated with effects on critical response sequences (Lv/Lv and Rn/Rn), information concerning drug effects on response sequences did not clarify differences in drug effects on response rate.

Effects of chlorpromazine. The effects of chlorpromazine on rate of responding are shown in Figure 3. Data are arranged as in Figure 1; effects for the three responses are arranged in columns and effects from the three schedule parameters are arranged in rows.

Chlorpromazine decreased rate of lever pressing in all schedule components for all three rats at 1.5 and 2.0 mg/kg. Lower doses produced no systematic effect on rate of reinforced lever pressing, but did produce effects on intercurrent responding. Unlike the effects on schedule-controlled lever pressing, however, the effects of chlorpromazine on both intercurrent responses were less consistent between subjects. Licking (center column) during the 20-sec IRT schedule (center row), for example, was decreased at larger doses for Rat 2 and Rat 3 but increased at the largest dose for Rat 1. Overall control rates of licking for Rat 1 and 2 were comparable. Differences also occurred in chlorpromazine ef-

ects on wheel running (right column). Low run rates for Rat 3 were increased by larger doses in all three schedule components. Comparably low run rates for Rat 1 and Rat 2 in the 10-sec IRT component (top row), and for Rat 1 in the 20-sec IRT component (center row), were not affected at any dose. In the case of effects on higher rates of running, responding by Rat 2 in the 20-sec and 60-sec IRT components was increased by intermediate doses of chlorpromazine and then decreased by larger doses. A high control-run rate for Rat 1 in the 60-sec IRT component, however, was not affected at any dose of chlorpromazine. Thus, the effects of chlorpromazine on reinforced lever pressing, like those of *d*-amphetamine, were consistent between animals and did not depend on drug effects on intercurrent responding: similar effects on the reinforced response were associated with different effects on intercurrent behavior.

Conditional probabilities among each of the three responses and for the response following food delivery were computed for each dose of chlorpromazine. As was the case for *d*-amphetamine, however, chlorpromazine effects on sequences including an intercurrent response were not consistent across animals and did not clarify individual differences for drug effects on rate of intercurrent responding. Also as with *d*-amphetamine, chlorpromazine effects on the response sequence "lever following lever" were the same for all animals and were positively correlated with effects on lever-press rate. These data are not presented.

Effects of chlordiazepoxide. The effects of chlordiazepoxide on response rates for Rats 2 and 3 only are shown in Figure 4. Rat R1 died from a presumed respiratory infection during early experiments with chlordiazepoxide. Data are arranged as in Figure 1. Chlordiazepoxide had virtually no effect on overall rate of reinforced lever pressing at doses up to 40 mg/kg, but had pronounced effects on intercurrent behavior at even the smallest dose. In addition, as was the case for *d*-amphetamine and chlorpromazine, drug effects on rate of intercurrent responses were different for different subjects, while effects on rate of reinforced responding were similar. Chlordiazepoxide effects on conditional probabilities did not clarify these differences, and the data are not shown. In the case of Rat 3, licking during the 10- and 20-sec IRT schedules was increased by

Fig. 4. Effects of chlordiazepoxide on mean rate of each response. Points are arranged as in Figure 1.

the smallest dose of chlordiazepoxide and decreased by the largest dose. Licking by Rat 2 during the same schedule components was unaffected at any drug dose. These differences did not appear to be related to differences in control rate of licking. Between-subject differences in chlordiazepoxide effects on rate of running did appear related to control rates, but the data are too limited to support general statements about rate-dependent effects.

Figure 5 shows effects of each drug (rows) on frequency of food presentation for each animal (columns). Comparison of a drug's effect on food frequency with its effect on rate of intercurrent responses shows that effects of *d*-amphetamine on food frequency and rate of licking were correlated for all three animals. However, there were no other systematic relations between effects of a drug on food frequency and rate of either intercurrent response.

DISCUSSION

The major finding of the present experiment is that lever pressing was similarly af-

Fig. 5. Effects of *d*-amphetamine (top row), chlorpromazine (middle row), and chlordiazepoxide (bottom row) on frequency of food presentation for each rat (columns). Unconnected points with vertical lines indicate the mean and range of five saline control sessions. Data points are mean values for the first 2 hr after a single injection of each dose.

ected by a given drug in all animals, while licking and running were generally affected differently by a given drug in different animals. Increasing doses of *d*-amphetamine first increased and then decreased rate of lever pressing maintained under the spaced-responding schedule of food presentation. Chlorpromazine produced dose-related decreases, and chlordiazepoxide had no substantial effect on rate of lever pressing up to a dose of 40 mg/kg. With the exception of chlordiazepoxide, these effects on lever pressing were consistent with previous reports of studies using similar schedules and drugs (e.g., Kelleher, Fry, Deegan, and Cook, 1961; Segal and Deadwyler, 1964; Sidman, 1955; Zimmerman and Schuster, 1962).

The finding that lever pressing was similarly affected by a given drug in all animals, while licking and running were generally affected differently in different animals, was probably not the result of different response topographies or different control response rates. Previous experiments have shown that, other things being equal, differences in response topography do not alter the major behavioral effects of meprobamate or *d*-amphetamine

(Kelleher *et al.*, 1961; Wuttke, 1970). It is unlikely that topography *per se* was any more critical in determining present drug effects. With respect to the importance of response rate, the widespread observation of rate-dependent drug effects suggests that rate of the various responses probably was implicated in certain of the present findings. For the most part, however, differences in rate of responses were not systematically related to a given drug effect and, hence, it is reasonable to conclude that response rate was not a singularly important determinant of the major finding.

In the present experiment, lever pressing by food-deprived rats produced food under a spaced-responding schedule; licking a tube and turning a wheel were recorded as intercurrent responses. Previous experiments have clearly demonstrated that drugs have consistent, orderly effects on adjunctive behavior (Byrd, 1973, 1974; McKearney, 1973; Segal and Deadwyler, 1964). The questions raised by the present data, then, are directed more at exploring conditions that define adjunctive behavior and considering contributions offered by behavioral pharmacology for the experimental analysis of intercurrent behavior.

A previous analysis of rates and patterns of responding by these animals suggested that, under these conditions, the classification of licking and running as adjunctive behaviors is specious (Smith and Clark, 1974). Although some of the functions relating response rate and sequence with schedule parameter were indicative of recurring patterns of intercurrent responding that define adjunctive behavior, others were not. And while recurring patterns of licking and running most certainly do occur under some conditions (*e.g.*, Falk, 1972; Skinner and Morse, 1957), they need not occur under all conditions. Whether or not they do probably depends upon preconditions such as deprivation, prior training, and the particulars of the ongoing schedule of reinforcement; the specificity of relations between the designated intercurrent responding and its consequences, and the schedule of presentation of those consequences. It is the combined property of all such conditions that induces the pattern of "other" responses which defines adjunctive behavior. In this experiment, licking the tube and turning the wheel were, by designation, maintained under less specific conditions than lever pressing. To be sure, every lick produced

a drop of water and every locomotor movement turned the wheel, and these consequences, combined with the schedule of food delivery, presumably maintained the licking and running. However, there was no manipulation of preconditions relevant to licking and running and there was no scheduled restriction on availability of water or access to the wheel.

It is generally recognized that different environmental conditions control different patterns of operant behavior. It is equally important to recognize that different conditions control different patterns of intercurrent behavior. Under some, very "powerful" conditions, specific recurring patterns of intercurrent responding are induced. Under other conditions, intercurrent behavior is more "loosely" controlled. When the former conditions are observed, drug effects have been consistent and orderly; when the later conditions are observed, as in the present experiment, drug effects are not consistent. However, it has often been recognized that drugs do not create new forms of behavior, but rather modify ongoing behavior (Kelleher and Morse, 1969, p. 396). It should not be surprising, therefore, that well-controlled, reproducible patterns of behavior are more consistently affected by any manipulation than is poorly controlled behavior (*cf.* Sidman, 1960, chapters 12 and 13).

With this recognition in mind, the present data recommend a more extensive analysis of intercurrent behavior. However, the analysis should no longer emphasize *a priori* conceptual differences between procedurally designated intercurrent and reinforced responses. Rather, the analysis should maintain a descriptive bias and seek to identify those conditions that engender a behavior (*e.g.*, Premack, 1965; Segal, 1972) and study the importance of scheduled consequences in maintaining that behavior (*e.g.*, Kelleher and Morse, 1968). As more is learned about comparative effects of drugs on schedule-controlled patterns of both intercurrent and reinforced responding, behavioral pharmacology will itself become a useful technique in the experimental analysis of intercurrent behavior.

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