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d-Amphetamine, Operant History, and Variable-Interval Performance[1]

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POLING, A., K. KRAFFT AND L. CHAPMAN. *d-Amphetamine, operant history, and variable-interval performance.* PHARMAC. BIOCHEM. BEHAV. 12(4) 559–562, 1980.—The effects of d-amphetamine on the bar-pressing of rats maintained under a variable-interval schedule of water reinforcement were examined as a function of the operant history of the subjects. One group of rats initially received 51 sessions of exposure to a fixed-ratio 20 schedule, while a second group received equivalent exposure to an interresponse-time-greater-than-12-sec schedule. Mean group response rate when stable was over ten times as high under the fixed-ratio schedule as under the interresponse-time-greater-than-12-sec schedule. Response rates of the two groups largely converged across 47 sessions of exposure to a variable-interval 60-second schedule, at which time response rates for both groups appeared stable. Acute administrations of d-amphetamine sulfate similarly affected mean response rates of both groups: A 0.25 mg/kg dose did not obviously affect rate, while doses of 0.5, 1.0, and 2.0 mg/kg produced dose-dependent rate decreases. These results indicate that the efficacy of operant history as a determinant of drug effects may be limited to circumstances where current contingencies do not exercise powerful and direct control over behavior.

d-Amphetamine Operant history Rate-dependent effects Fixed-ratio schedule
Variable-interval schedule Interresponse-time-greater-than-t schedule Lever-press Rats

THE behavioral effects of many drugs depend critically on the rate of occurrence of the behavior in the absence of the drug [9,19]. For example, d-amphetamine in low-to-moderate doses typically produces "rate-dependent effects", [4, 5, 19] increasing low-rate behaviors while decreasing high-rate behaviors (e.g., [3, 4, 5, 17, 23]).

Many factors affect the rate of occurrence of a particular behavior. Reinforcement schedules exercise strong control over response rates [6,26] and studies of drug effects under various reinforcement schedules have been quite informative [9,12]. Since drug effects often are dependent on nondrug response rates, which are determined by the reinforcement schedule maintaining behavior, drug effects are indirectly schedule-dependent [14].

However, response rate under a given schedule is affected by several factors, including a history of responding under a different schedule [6, 23, 24, 25]. The effects of such a history can be strong and enduring: Urbain, Poling, Millam, and Thompson [23] demonstrated that rats with a conditioning history under fixed-ratio (FR) schedules produced high rates of responding under fixed-interval schedules (FI), while subjects with a history under interresponse-time-greater-than-t (IRT>t) schedules produced far lower rates under identical FI schedules. Such a difference in response rates under the FI should influence the manner in which rate-dependent drugs affect fixed-interval performance, and this occurred when d-amphetamine was given. At doses of 0.25, 0.5 and 1.0 mg/kg, this compound generally increased response rates under the FI schedule when administered to animals with IRT>t histories, but decreased FI response rates when given to rats with FR experience. This indicates the potential importance of historical factors as determinants of drug effects, and emphasizes that the behavioral actions of a drug in a given situation are by no means qualitatively or quantitatively fixed.

However, response rate under the fixed-interval schedule is particularly sensitive to what Zeiler ([26] p. 204) termed "indirect" variables, i.e., variables that are imposed without being directly prescribed by the schedule. Insofar as behavioral history is an indirect variable, its effects are likely to be more pronounced under a fixed-interval schedule than under schedules where control by indirect variables is overshadowed by formal impositions of the schedule ("direct" variables). It is unclear to what extent responding under such schedules, and resultant sensitivity to d-amphetamine, would be influenced by operant history [23]. In order to evaluate the generality of behavioral history as a determinant of drug effects, the present study assessed whether d-amphetamine would differentially affect the variable-interval (VI) performance of rats given FR or IRT>t histories.

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METHOD

Subjects

Twelve experimentally-naive adult male Sprague-Dawley rats were used. The subjects were water-deprived to approximately 85% of nondeprived weights by limiting weekday home-cage access to water to 10 min immediately following experimental sessions, and limiting weekend consumption to 50 ml, presented immediately after the Friday session. They were individually housed with free access to food, and were maintained in accordance with the general principles of animal husbandry promulgated by the National Research Council [15].

Apparatus

Two modified Gerbrands rodent conditioning chambers, enclosed in sound-attenuating cubicles, were used. The front panel of each chamber was 20×10-cm and was equipped with a 0.15-ml capacity liquid dipper accessible through a 4-cm opening horizontally centered 4-cm above the chamber's floor. When desired, the dipper was lowered and filled with water. A response level, operated by a downward force of at least 0.2 N, was located on the front panel 6 cm from the right side wall. An exhaust fan provided ventilation and masking noise. Electromechanical equipment located in an adjoining room arranged experimental events and recorded data.

Procedure

Throughout the experiment, sessions were 30 min in length and were conducted five days per week, at the same time each day. Each rat initially was trained to lever-press under a fixed-ratio 1 (FR 1) schedule, where delivery of the water-filled dipper followed each response. When all subjects responded consistently under this schedule, they were randomly divided into two groups of six. For one group, the FR value was increased gradually to a maximum value of 20; the second group was exposed to an interresponse-time-greater-than-12 sec (IRT>12-sec) schedule. Under the IRT>12-sec schedule, at least twelve seconds had to elapse between responses before water was delivered; premature responses reset the interval.

The FR 20 and IRT>12-sec schedules were in effect until mean group response rates were stable across five consecutive sessions, with stability defined as mean group response rate during sessions N, N+1, and N+2 being within ± 5% of the rate obtained during sessions N+2, and N+3, and N+4. Response rates first stablized for both groups during sessions 47–51.

At the beginning of session 52, all subjects were exposed to a variable-interval 1-min (VI 1-min) schedule of water reinforcement. Under this schedule, responses were followed by water once per minute, on the average, although the time between consecutive dipper presentations varied irregularly from 5-sec to 4-min. Ten minutes prior to sessions in which the VI schedule was in effect, subjects were injected intraperitoneally with 0.9% isotonic saline solution (1 ml/kg of body weight). One day after response rates under the VI schedule were stable across 5 consecutive sessions (above), a drug regimen was begun. Response rates first stabilized during sessions 43 to 47 of VI exposure.

During the drug regimen, d-amphetamine sulfate, dissolved in isotonic (0.9%) saline solution to an injection volume of 1 ml/kg of body weight, was intraperitoneally injected twice each week, with drug sessions separated by at least two saline control sessions. Drug injections were given 10 minutes before the start of the session. Each subject received d-amphetamine doses of 0.25, 0.5, 1,0, and 2.0 mg/kg (doses refer to the total salt). Doses were administered in an irregular sequence, and each rat received each dose on two occasions. During every session, number of responses emitted and number of dipper presentations were recorded.

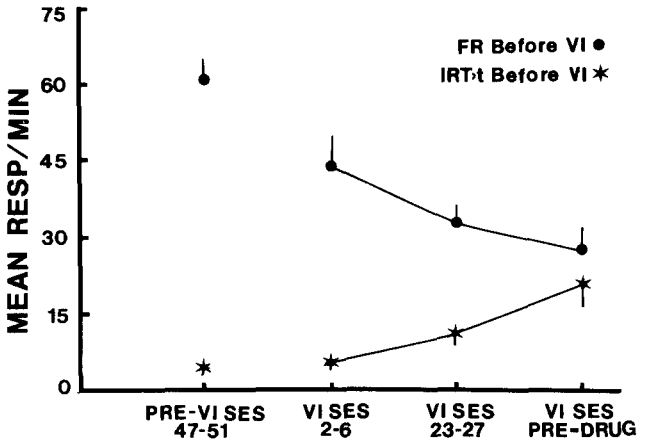

FIG. 1. Mean group response rates during the final five sessions of exposure to the FR 20 or IRT>12-sec schedule (pre-VI), and at various stages of exposure to the VI 60-sec schedule. Pre-drug rate represents sessions 43–47 of VI exposure, when rates for both groups were stable. Each data point represents the mean performance of six subjects; vertical lines indicate 1 standard error.

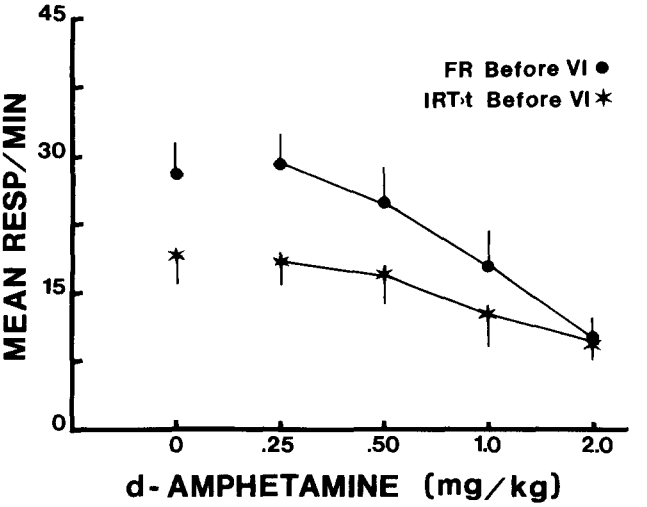

FIG. 2. The effects of d-amphetamine on the VI 60-sec performance of rats with FR 20 or IRT>12-sec histories. Each drug data point (0.25, 0.5, 1.0, and 2.0 mg/kg) represents mean responses per minute across 12 sessions (6 rats×2 administrations of each dose), while each control data point (0 mg/kg) indicates the mean rate obtained during the 48 sessions that immediately preceded drug administrations (6 rats×2 administrations of each dose×4 doses). The vertical lines signify 1 standard error.

RESULTS

The mean group response rate under the FR 20 schedule was over ten times as high as the mean group response rate

under the IRT>12-sec schedule, as shown in Fig. 1 (pre-VI sessions). As this figure also shows, response rates of the two groups steadily converged with increasing exposure to the VI schedule, although the mean group response rate of animals with FR histories remained higher throughout the study. The convergence that occurred reflected both a decrease in the response rate of animals with FR histories and an increase in the response rate of animals with IRT>t histories; the absolute magnitude of the former decrease was larger than that of the latter increase. Although the response rate of the two groups differed during nondrug VI sessions, this difference did not affect the number of reinforcers earned: Both groups consistently received over 95% of the available reinforcers.

The effects of d-amphetamine on VI 60-sec performance for subjects with FR 20 and IRT>12-sec histories are shown in Fig. 2, where data are expressed as mean response rate for each group during drug and saline control sessions. Dose-response curves for the two groups were much alike, although most drug doses more strongly affected the performance of animals with FR histories. For both groups, the lowest dose of d-amphetamine (0.25 mg/kg) affected response rate very little; higher doses produced dose-dependent decreases in mean response rate. A repeated measures analysis of variance indicated that overall drug effects were significant for animals with FR histories ($F=5.2$, $p<0.01$) and for animals with IRT>12-sec histories ($F=6.6$, $p<0.01$). Newman-Keuls comparisons [10] of control response rates with the rates obtained under each drug dose indicated that, for both groups, d-amphetamine significantly ($p<0.05$) decreased responding at doses of 1.0 and 2.0 mg/kg. Across all doses and animals, d-amphetamine reduced the response rate of individual animals with FR histories relative to mean control values in 38 of 48 instances (6 animals×2 administrations×4 doses), while in 30 of 48 instances the response rate of individual animals with IRT>12-sec histories was lowered by the drug.

DISCUSSION

As in previous studies [23, 24, 25], response rates were much lower under the IRT>t schedule than under the FR schedule. In the present experiment, response rates of animals given IRT>t and FR histories converged rapidly and strongly upon subsequent exposure to the same reinforcement schedule. An earlier study [23] also demonstrated such convergence, although the magnitude of the effect was less than in the present study. The difference in the degree of convergence obtained probably reflects the final schedule to which the rats were exposed: The previous experiment [23] exposed animals to an FI schedule after IRT>t or FR experience, while the terminal schedule in the present study was VI.

Characteristic FI performance consists of a low overall response rate with a positively accelerated pattern of responding ("scalloping") within individual intervals [6], although the formal characteristics of this schedule are such that a wide range of response rates will produce all of the available reinforcers [26]. Because of this, response rates under the FI schedule vary widely across subjects given no special training (e.g., [8]), and also are affected strongly by "indirect" variables [26] such as operant history [23, 24, 25].

In contrast to typical FI performance, the VI schedule usually generates a moderately high rate and stable pattern of responding [6]. This schedule specifies that reinforcers follow responses at irregular and unsignalled intervals, therefore low-rate and inconsistent patterns of responding are relatively ineffective with respect to total reinforcers earned. The VI schedule constrains performance more tightly than does the FI schedule, although certain other schedules exercise greater direct control over rate and pattern of responding that does the VI. The FR schedule, for example, specifies a direct relation between response rate and reinforcement density. This schedule engenders high response rates in most subjects [6]. Zeiler [26] discusses in detail the factors that control responding under various reinforcement schedules.

In the present study, d-amphetamine similarly affected the VI performance of rats with FR and IRT>t histories. No qualitatively different effects were apparent (cf., [23]), and the quantitative differences that were observed were not impressive. Although a previous study [23] found that d-amphetamine produced dissimilar effects on the FI performance of rats given FR and IRT>t experience, this was not the case under the VI schedule.

Drug effects on responding maintained under VI schedules have not been studied extensively, but previous reports have found that amphetamines can both increase and decrease response rates under such schedules [4, 7, 13, 18, 21, 22]. Specific rate-dependent effects under VI schedules have been reported [5, 11, 20], and it generally is assumed that rate-dependent effects will occur whenever (local) response rates vary across a relatively wide range (see [5,19] for reviews of rate-dependency). If in the present study d-amphetamine had been administered following relatively brief exposure to the VI schedule, when the response rates of rats with FR and IRT>t histories differed greatly, operant history might well have demonstratively influenced drug effects. However, after VI performance had stabilized, this did not occur. The present findings thus support earlier suggestions [16,23] that operant history is an indirect variable that influences the behavioral actions of a drug under some, but certainly not all, schedules of reinforcement. Despite this, it should be emphasized that operant history as a determinant of drug effects has been explored in little detail. Operant history did not strongly influence drug effects in the present experiment, but earlier studies using similar [23] and different [1, 2, 16] paradigms have demonstrated conclusively that an animal's past experiences can be a potent determinant of the outcome of drug administration. The range of conditions under which this occurs is in need of further exploration.

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