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Methamphetamine Effects on Responding under a Multiple Schedule of Shock Presentation[1]

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MCKEARNEY, J. W. *Methamphetamine effects on responding under a multiple schedule of shock presentation.* PHARMAC. BIOCHEM. BEHAV. 1(5) 547–550, 1973.–Squirrel monkeys responded under a multiple 3-min variable-interval (VI) 10-response fixed-ratio (FR) schedule of response-dependent electric shock presentation. Methamphetamine (0.01–0.17 mg/kg) produced dose-dependent increases in relatively low rates of responding whether these occurred during the FR or the VI component of the schedule. In the one monkey with a relatively high control rate of responding during the VI component, methamphetamine only produced decreases in responding. Responding during the FR component was increased by methamphetamine, even in the monkey whose responding appeared to be suppressed during this component. Previous experiments have shown only further decreases after amphetamines in responding suppressed by response-dependent shock. The present experiments indicate that, in addition to the frequency and intensity of the electric shock and to the schedule maintaining the reference behavior, the nature of the event maintaining the reference behavior can be important in determining the effects of amphetamines. The effects of methamphetamine depend not only on the intensive and temporal characteristics of the ongoing schedule-controlled behavior itself, but also on the past and present context in which the behavior occurs.

Methamphetamine Shock presentation Variable-interval Fixed-ratio Maintenance by shock Suppression Squirrel monkey

THE effects of amphetamines on schedule-controlled behaviors depend on the control rate of occurrence of the behavior; relatively low rates of responding are increased at doses that have little effect, or may even decrease, higher rates of responding. Though it is generally true that amphetamines increase low rates of responding, there are conditions under which this effect is modified. For example, behaviors with an extremely low probability of occurrence [19,24] or behaviors under control of strong discriminative stimuli [13] may be resistant to increase. Another important exception is that amphetamines do not generally increase rates of responding suppressed by presentation of an aversive stimulus such as electric shock (punishment) [6].

A number of experiments have demonstrated that, under certain conditions, responding can be maintained rather than suppressed under procedures in which the only consequence of responding is the presentation of an intense electric shock [2, 10, 14, 22] and that characteristic performances are maintained under a variety of schedules of shock presentation [15, 16, 17]. Further, in contrast to effects on punished responding, *d*-amphetamine produces dose-dependent increases in responding under a fixed-interval (FI) schedule of shock presentation, just as it does under FI schedules of food or water presentation [18].

Kelleher and Morse [10] have demonstrated that electric shock of a given intensity can either maintain or suppress responding, depending on the schedule of presentation; responding was maintained when shocks were presented under a fixed-interval schedule, but suppressed when a shock followed every response. More recently, McKearney [17] has shown that in monkeys responding under a variable-interval schedule of shock presentation, responding is suppressed when electric shocks follow every response during certain portions of the session. The present experiments made use of a procedure similar to that reported earlier [17].

In the experiments reported here, squirrel monkeys, with an experimental history under various schedules of shock postponement and shock presentation, responded under a multiple 3-min variable-interval, 10-response fixed-ratio schedule of response-dependent electric shock presentation. Methamphetamine produced dose-dependent increases in relatively low rates of responding during both components of the schedule, even when responding appeared to be suppressed by electric shock delivery.

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METHOD

Animals and Apparatus

One male (S-65) and one female (S-184) adult squirrel monkey (Saimiri sciureus) had both been used in previous experiments involving various schedules of shock postponement and shock presentation. The monkeys were housed individually and were handled according to the general procedures reported by Kelleher, Riddle, and Cook [12].

Experiments were conducted with individual monkeys seated in a restraining chair [7,8]. The monkey's tail was held motionless by a small stock, and electric shocks were delivered through brass electrodes that rested on a shaved portion of the tail. The shock was 650 V a.c., 60 Hz, of 200-msec duration, delivered to the electrodes through variable series resistance. The response key (Lehigh Valley Electronics rat lever, LVE 1352) was mounted on a wall facing the monkey. Each depression of the response key with a force of approximately 20 g (0.196 N) or more produced the audible click of a relay within the chamber, and was recorded as a response. The restraining chair was enclosed in a sound-attenuating chamber. Two 7.5-W white lights illuminated the chamber during sessions. Continuous white noise was present to mask extraneous sounds.

Procedure

In earlier experiments [15, 16, 17] both monkeys had been trained under a continuous avoidance schedule [23] and were then exposed to various schedules in which the only consequence of responding was the presentation of an electric shock. In all cases, the performances engendered were appropriate to the schedules in operation.

In the experiments to be reported here a 3-min variable-interval schedule of shock (5 mA) presentation was in effect in the presence of white light; that is, an electric shock was presented following the first response to occur after the passage of a variable period of time averaging 3 min. Sessions were conducted five days per week and were normally terminated after the thirtieth shock presented under the VI schedule.

During min 9, and for a 1-min period every 10 min thereafter, of each daily session, the color of the lights in the chamber was changed to orange, and a shock was presented following every tenth response during these periods. This is a 10-response fixed-ratio (FR) schedule, and the entire procedure is a multiple 3-min variable-interval, 10-response fixed-ratio schedule of shock presentation. For S-184, all shocks delivered under both components were response-produced. For monkey S-65 only, a continuous avoidance schedule was concurrently in effect during both schedule components; under the avoidance schedule, shocks were scheduled to be delivered every 5 sec, but each response postponed avoidance shock for 25 sec.

Methamphetamine HCl (courtesy of Burroughs-Wellcome and Co.) was dissolved in 0.9% sodium chloride solution and was prepared at several concentrations so that the volume injected was 1.0 ml/kg body weight. Doses were given in mixed order, and are expressed in terms of the salt. Injections were intramuscular, immediately before the session. Drugs were normally given on Tuesdays and Fridays, with Thursday's performance serving as control. Drug effects are expressed as absolute changes in response rate during VI and FR components. Statistical significance of changes in response rate were determined by *t*-tests.

RESULTS

Control Performances

As reported previously [17] characteristic variable-interval patterns of responding [4] were maintained under the 3-min VI schedule of shock presentation. The average rate of responding during the VI component was 1.73 (SD = 0.095) responses/sec for S-65 and 0.62 (SD = 0.055) responses/sec for S-184. During the FR 10 component, control response rates were 0.036 (SD = 0.023) and 0.676 (SD = 0.071) responses/sec for S-65 and S-184, respectively. Thus, for S-65 responding during the FR component was suppressed relative to VI responding while for S-184 response rate was higher during the FR than during the VI component.

Monkey S-65 received an average of approximately three shocks/session under the avoidance schedule which operated concurrently with the multiple schedule of shock presentation. The presence of the avoidance schedule undoubtedly accounts for the much higher rate of VI responding observed in this monkey.

Methamphetamine Effects

Figure 1 summarizes the effects of methamphetamine on responding during the VI and FR components, and Fig. 2 shows cumulative response records for S-184 under control conditions and after 0.17 mg/kg methamphetamine.

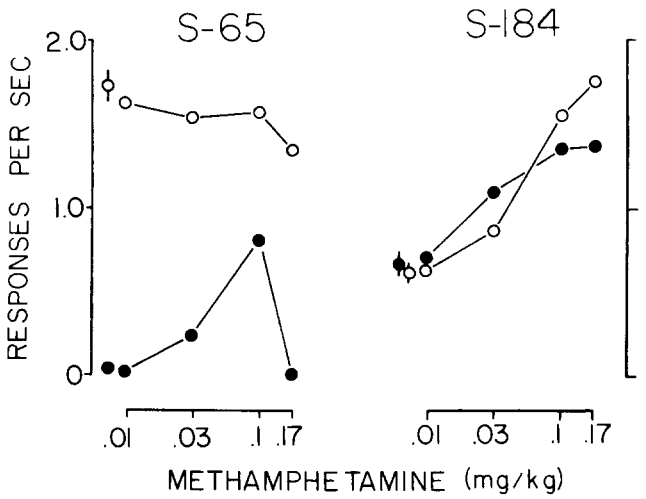

FIG. 1. Methamphetamine effects on responding under a multiple 3-min variable-interval 10-response fixed-ratio schedule of shock presentation. Open circles: VI. Filled circles: FR. Unconnected points at left of each plot are average rates under control (no drug) conditions; vertical lines represent ± one standard deviation (except where this falls within the area covered by the data point). Each point represents a single observation except that data for S-184 at 0.03 and 0.1 mg/kg are averages of two observations. Note that methamphetamine increased relatively low rates of responding in both components, but only decreased higher rates.

For S-65, whose control rate of responding in the VI component was quite high (1.73 responses/sec), methamphetamine had little effect at lower doses and decreased responding ($p<0.01$) at the highest dose. For S-184, however, whose control rate of responding in the VI component

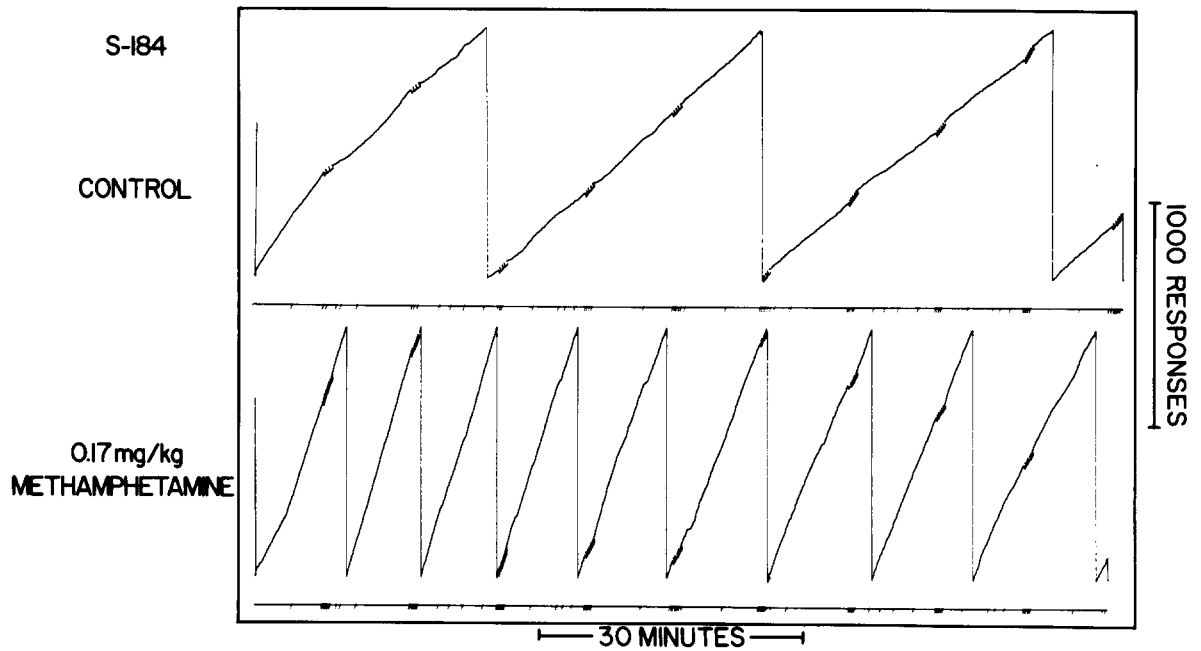

FIG. 2. Effects of methamphetamine (0.17 mg/kg) on responding under a multiple 3-min variable-interval 10-response fixed-ratio schedule of shock presentation (monkey S-184). Ordinate: cumulated responses. Abscissa: time. The recording pen was displaced downward during fixed-ratio (FR) components. All shocks were recorded as downward deflections of the event marker, and shocks during FR periods are indicated by an upward deflection of the recording pen as well. Note that methamphetamine increased responding under both schedule components.

was relatively low (0.62 responses/sec), methamphetamine produced dose-dependent increases in responding ($p<0.001$) at 0.03, 0.1 and 0.17 mg/kg.

In both monkeys there were dose-dependent increases in responding during the FR 10 component of the schedule. For S-184 there were increases in FR 10 responding ($p<0.001$) at all but the lowest dose. For S-65 there were significant increases in FR responding at 0.03 ($p<0.01$) and 0.1 mg/kg ($p<0.001$), and a return to control values at the highest dose. For S-65, the number of shocks received under the concurrent avoidance schedule was unchanged from control (3.3/session) at lower doses of methamphetamine, but increased after 0.1 mg/kg (13.0/session) and 0.17 mg/kg (51.0/session).

DISCUSSION

In spite of differences in procedure and in control rates of responding for the two monkeys, both showed marked increases in low rate responding that produced shock, even when, in the case of S-65, responding appeared to be suppressed by shock presentation.

Methamphetamine produced dose-dependent increases in relatively low rates of responding whether these occurred during the FR component (both monkeys) or the VI component (S-184) of the multiple schedule of shock presentation. Relatively high rates of responding during the VI component (S-65) were only decreased by methamphetamine. These results are consistent with previous reports of an inverse relation between control rate and magnitude of increase produced by amphetamines [3, 9, 19]. Further, these results complement a previous report [18] showing that the same inverse relationship applies to *d*-amphetamine effects on responding under a fixed-interval schedule of electric shock presentation.

For S-184, responding was not suppressed during the schedule component (FR) in which every tenth response was shocked; in fact, response rate was slightly higher here than during the VI component. The increases in FR responding seen after methamphetamine were not unexpected in view of the well documented tendency of amphetamines to increase low and moderate rates of responding regardless of the particular reinforcement schedule [20] or the nature of the reinforcer [8].

For S-65, on the other hand, response rate was extremely low during the FR component under control conditions (0.036 responses/sec, or about 2.2 responses per 1-min FR period). Since responding was so low relative to that during VI, it might be assumed that this responding was suppressed by punishment, as usually defined [1]. The dose-related increases in this low-rate responding, however, lead to some question of this assumption, and of the advisability of defining suppression or punishment solely in terms of the emergence of a lowered rate of responding. Though a low rate of responding under a schedule of response-dependent shock could indicate response suppression, it may instead reflect a maintenance of responding at that low rate, especially under procedures in which shock is maintaining behavior in another schedule component. When responding is suppressed by shock, amphetamines usually further decrease responding, but when responding is maintained, albeit at a low level, amphetamines may increase this responding.

While most experiments have shown only further decreases in punished responding after amphetamines [6,9], there are apparently some conditions under which

amphetamine can increase punished responding. McMillan and co-workers [5,21] found that *d*-amphetamine could increase low rates of punished responding (in the early segments of a fixed interval) which have not resulted from severe punishment. These and other experiments suggest that the effects of amphetamines on punished responding depend on the control rate of responding which, in turn, is determined by the punishment intensity and frequency and by the schedule maintaining the reference behavior. The present experiments indicate, in addition, that the nature of the event maintaining the reference behavior (and any similarities it may bear to the event serving as the punisher) can also be important in determining the effects of amphetamines. Though the effects of a given event may be different, in that it may either maintain or suppress responding depending on the schedule of presentation [10, 11, 17] this does not necessarily mean that the effects of drugs on the behaviors maintained or suppressed will be different. The effects of drugs depend not only on the intensive and temporal characteristics of the ongoing schedule-controlled behavior itself, but also on the past and present context in which the behavior occurs.

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