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Differential Effects of Methylphenidate on Signalled and Non-Signalled Reinforcement[1]

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EMMETT-OGLESBY, M. W., K. E. TAYLOR AND R. E. DAFTER. *Differential effects of methylphenidate on signalled and non-signalled reinforcement.* PHARMAC. BIOCHEM. BEHAV. 13(3) 467–470, 1980.—Rats were trained to press a bar with water reinforcement under a variable interval 15-sec (VI 15), variable interval 15-sec signalled-reinforcement (VI S^D), or a differential-reinforcement-of-low-rate 10-sec (DRL 10) schedule. Methylphenidate (MP) had little effect on response rates or reinforcements-earned in the VI 15 group. However, MP increased response rates in a dose-related manner in the VI S^D and the DRL 10 groups. These findings and additional results reported in the literature suggest that signalled reinforcement does not necessarily antagonize the rate-increasing effects of the amphetamine-type drugs.

Stimulus control Signalled reinforcement Methylphenidate Extinction

AMPHETAMINES typically increase low rates of responding; however, low rates of responding associated with the extinction portion of S^D–S^Δ paradigms have been reported to be resistant to rate-increasing effects of amphetamines [2, 4, 13]. These and additional results have been summarized in recent reviews concluding that behavior under strong stimulus control is insensitive to the disruptive effects of many drugs [10,12].

Not all studies have verified this observation. Clark and Steele [3] found that amphetamine increased response-rates in rats during the extinction portion of a multiple schedule, and subsequent studies have reported similar results [6,14]. In reconciling these results with those described above, it has been suggested that if a tendency exists to respond during S^Δ, then amphetamines will produce rate-increasing effects. The studies of Thompson and Corr [13] and T'so *et al.* [14] illustrate this principle.

Thompson and Corr used a variable interval one-minute schedule of reinforcement with a stimulus associated with the availability of reinforcement. Operationally, this is equivalent to a multiple schedule of S^D–S^Δ in which fixed-ratio-one (FR 1) reinforcement alternates with variable-duration extinction that averaged one-minute [5]. Pigeons trained under this schedule eventually emitted nearly all responses only when reinforcement was signalled. Responses in the extinction phase did not exceed 0.4 responses per minute, and *d*-amphetamine did not increase these low rates of responding. T'so *et al.* trained rats under a multiple schedule of food reinforcement in which a 1-sec stimulus signalled the start of 8-sec FR 1 access followed by variable-duration extinction (EXT) that averaged 36 sec. Discrete stimuli did not differentiate the 8-sec FR1 and EXT components, and perhaps because of this training procedure, approximately 3 responses per minute occurred during extinction; as opposed to the results of Thompson and Corr, *d*-amphetamine (*d*-A) increased response-rates in a dose related manner.

T'so *et al.* also used methylphenidate (MP) in doses up to 5 mg/kg and found that it had little effect on response rates in extinction. This result may have been a consequence of using too limited a dose-range of MP, because MP and *d*-A have been shown to produce essentially interchangeable effects [1, 7, 9] with *d*-A approximately 6 to 8 times more potent than MP.

The present study investigated the effects of MP on response rates of rats trained under signalled and non-signalled reinforcement procedures. Signalled reinforcement was used to obtain a high degree of stimulus control over responding,

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and a wide range of doses of MP were employed in order to test fully the rate-increasing properties of this drug in signalled and non-signalled responding.

METHOD

Subjects

Twenty-four experimentally naive, male, Sprague-Dawley (Holtzman Co.) rats, 60 days old at the beginning of experiments, were subjects. All animals were housed in pairs and received ad lib food (Purina Rat Chow) in their home cages. Body weights were maintained at 300 ± 5 g throughout the experiment by restricting access to water. All rats received approximately 1 ml of water in daily behavioral sessions and 19 ml of supplemental water in their home cages immediately after each session.

Apparatus

Eight experimental chambers (30×46×30 cm) (Rayfield Equipment Co., Chicago) were enclosed in sound and light attenuating boxes. Houselight was provided by a 2.5 W bulb mounted on the ceiling. Exhaust fans ventilated the chambers and masked extraneous sounds. Each chamber contained a single response lever, 10.5 cm above the mesh floor, mounted on a wall to the left of a small opening permitting access to a 0.01 ml capacity dipper. Depressing the lever closed a microswitch and activated the dipper. Rayfield digital logic modules programmed the experimental events and recorded the data.

Procedure

All rats were trained to bar press with water as a reinforcer and then trained for three 20-min sessions on a continuous reinforcement schedule under which every bar press was reinforced. Subsequently, each subject was assigned randomly to one of three conditions, 8 rats per group. One group responded under a variable-interval 15-sec (VI 15) schedule in which reinforcement was contingent on the first response following a variable interval that averaged 15 sec. A second group also responded under a VI 15 schedule, but the chamber lights flashed at 3 Hz when reinforcement was available (VI S^D). Under this schedule, the first response in the signal component produced S^R and terminated the signal. On the average, approximately 4 signal opportunities occurred each minute, and a response rate of 4 per minute indicates nearly ideal matching of responses to the S^D. The third group was trained on a differential-reinforcement-of-low-rate 10-sec (DRL 10) schedule in which only responses made following 10 or more seconds of non-responding were reinforced.

All subjects were run five days per weeks, 2 hr per session. Beginning with the 26th session, all subjects were injected intraperitoneally (IP) 20-min pre-session with 0.9% saline, 1 ml/kg, and this regimen was continued for three sessions. Subsequently, doses of 5, 10, 20 and 33 mg/kg of MP were injected IP to all subjects, 20-min presession. At least four non-drug sessions elapsed between each dose determination. The control rate of responding and reinforcement acquisition was determined from the last three consecutive sessions prior to saline testing.

Drug

Methylphenidate HCL (CIBA-GEIGY, Summit, NJ) was dissolved in 0.9% saline and injected in a volume of 1 ml/kg. Doses refer to weight of the salt.

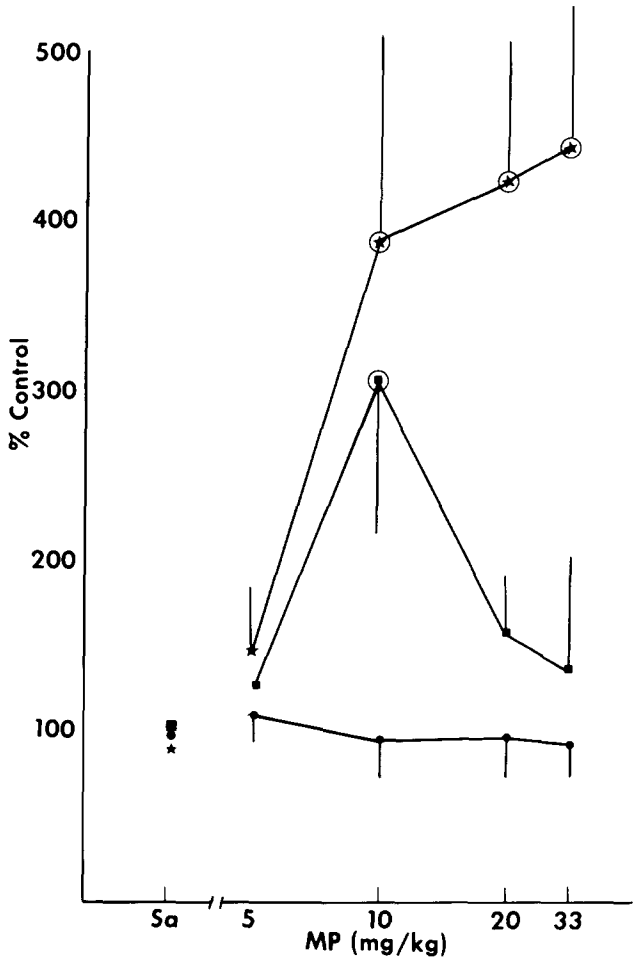

FIG. 1. Effect of methylphenidate on rate of responding. Ordinate: percent of control rate. Control values are the averages for each group obtained from the last three sessions prior to the initiation of drug testing. Abscissa: saline (Sa) or doses of methylphenidate. Bars denote standard error of the mean. Circled points are significantly different from their saline points. Group symbols and control rates ± SD: ●=VI 15, 84.3 ± 39.0; ★=VI S^D, 5.1 ± 0.1; ■=DRL 10, 5.0 ± 1.2.

RESULTS AND DISCUSSION

Because of equipment failure, schedule control was not established for two rats in the VI S^D condition, and they were dropped from the experiment. By session 24, rats in the VI S^D and DRL 10 groups developed uniformly low rates of responding. Control rates during sessions 21 through 24 for individual rats in the VI S^D group ranged from 5.0 to 5.2 responses per minute. Thus, responding was under strong signal control; approximately 4 responses per minute were associated with reinforcement and one response per minute occurred during S^Δ. In contrast, the non-signalled VI 15 produced response rates that varied between rats from 30 to 150 responses per minute.

The interaction effect was significant in a 3×5 repeated measures analysis of variance for the effect of MP on response rate, $F(8,68)=2.13$, $p<0.05$. Direct tests on main ef-

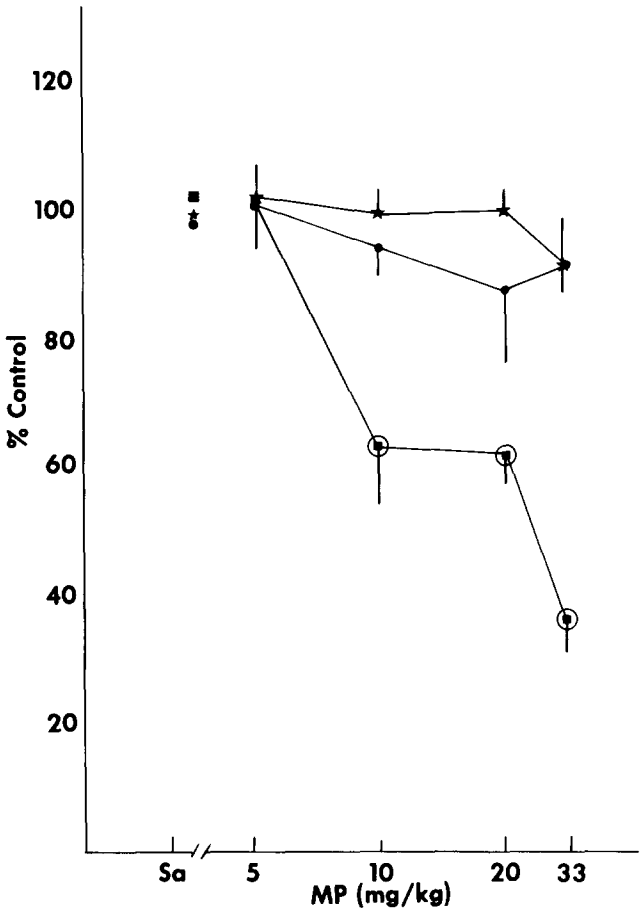

FIG. 2. Effect of methylphenidate on reinforcements obtained. Ordinate: percent of control number of reinforcements. Control values are the averages for each group obtained from the last three sessions prior to the initiation of drug testing. Abscissa: saline (Sa) or doses of methylphenidate. Bars denote standard error of the mean. Circled points are significantly different from their saline points. Group symbols and control reinforcements ± SD: ●=VI 15, 498 ± 57; ★=VI S^D, 458 ± 36; ■=DRL 10, 397 ± 94.

fects showed that MP significantly increased responding in the VI S^D, $F(4,20)=8.1$, $p<0.01$, and DRL, $F(4,28)=2.73$, $p<0.05$, groups; effects that differed significantly from saline were identified by Newman-Keuls tests (Fig. 1). The increased rate of responding in the DRL 10 group resulted in a decrease in reinforcements earned (Fig. 2). The interaction effect in a 3×5 repeated measures analysis of variance was again significant, $F(8,68)=4.4$, $p<0.01$, and tests on main effects showed that MP significantly decreased reinforcers obtained in the DRL 10 group, $F(4,28)=25.3$, $p<0.01$.

Responding in the VI 15 group occurred at a relatively high rate, and MP essentially had no effect on either response rate or number of reinforcements received. These results are in agreement with previous studies suggesting that amphetamine-type drugs have little effect on operant responding controlled by low-value VI schedules [8]. Similarly, these results are also in accord with studies demonstrating that amphetamine-type drugs increase response rate and decrease reinforcements earned under DRL schedules [9,11]. However, the finding that MP increased response rates in the VI S^D group is not consistent with results reviewed by Sanger and Blackman [10] and Thompson [12] showing that stimulus control of responding either eliminated or greatly attenuated the rate increasing effects of amphetamines.

One possibility that may account for different results is that the degree of stimulus control of responding varies among experiments. Thompson [12] and Kelleher and Morse [8] have suggested that if a certain tendency to respond during S$^\Delta$ is present, then stimulus control may be disrupted by drugs. However, Thompson and Corr [13] used a signalled reinforcement procedure in which pigeons emitted approximately 10 to 25% of their responses during S$^\Delta$; this upper value is comparable to the percentage of S$^\Delta$ responses obtained in the present study, but different drug effects were obtained between the studies. In addition, in one study in which rats were resistant to rate increasing effects of amphetamine, very poor stimulus control was obtained [2]; nearly as many responses were emitted in the non-reinforced component as during the reinforced component. Thus, if the degree of stimulus control is a critical variable in preventing drug-induced increases in S$^\Delta$ responding, then the conditions under which it consistently produces this effect have yet to be specified.

As reviewed by Sanger and Blackman [10] and Thompson [12], most experiments reporting decreased drug effects with stimulus controlled responding have used pigeons as subjects. Only one experiment using rats has verified this phenomenon [2], and as described above, the degree of stimulus control was such that interpretation of these results is difficult. On the other hand, in addition to the present results, studies have shown that S$^\Delta$ responding in rats is increased by amphetamines [3, 6, 14], and little information is available with regard to other species. Thus, the degree to which stimulus control modifies drug effects should be examined further within the context of species variability.

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