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The Effects of Amphetamine on a Multitrial Partial Reinforcement Extinction Effect (PREE) in an Operant Chamber

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FELDON, J. AND I. WEINER. *The effects of amphetamine on a multitrial partial reinforcement extinction effect (PREE) in an operant chamber.* PHARMACOL BIOCHEM BEHAV 32(1) 65–69, 1989.—Two experiments investigated the effects of d-amphetamine (1 mg/kg) on the partial reinforcement extinction effect (PREE) in an operant chamber using a discrete multitrial procedure. Experiment 1 used a random 50% partial reinforcement (PRF) schedule. Experiment 2 used two 40% PRF schedules: one schedule maximized the number of nonreinforced trials preceding any given reinforced trial (maximum N-length of four) and the second maximized the number of N-R transitions (N-length of one). In both experiments, the continuously reinforced (CRF) animals received a reward on every trial. The PREE, i.e., increased resistance to extinction of PRF as compared to CRF animals, was obtained in the random 50% PRF and the schedule maximizing N-length in both the placebo and amphetamine-treated animals. Both drug and no-drug animals failed to exhibit PREE on the schedule maximizing N-R transitions. These results show that on a PRF schedule with short intertrial intervals, amphetamine-treated animals are not impaired in their capacity to learn sequences of events and to associate the outcomes of preceding trials with subsequent consequences.

d-Amphetamine Partial reinforcement Continuous reinforcement Extinction Rat

THE partial reinforcement extinction effect (PREE) refers to increased resistance to extinction of partially reinforced (PRF) as compared to continuously reinforced (CRF) animals. In a series of previous experiments investigating the effects of amphetamine on the PREE in a runway, we found that the effects of amphetamine on the PREE were determined by the intertrial interval (ITI). Thus, the drug disrupted the PREE when training consisted of 1 trial per day (7,8), but left the PREE intact when a multitrial training procedure (6 daily trials with 5-min ITI or 3 daily trials with 20-min ITI) was used (2). The present experiments sought to examine the generality of the latter finding across experimental situations as well as to test the effects of additional experimental parameters on the development of a multitrial PREE under amphetamine. Two experiments were conducted using an operant analogue of the runway discrete trial procedure. Experiment 1 used a random 50% partial reinforcement schedule. Experiment 2 manipulated two parameters of the partial reinforcement training which are considered critical in determining the magnitude of resistance to extinction at short ITI's, namely, the number of transitions from nonreinforced to reinforced trials over the course of acquisition (N-R transitions) and the number of nonreinforced trials preceding any given reinforced trial (N-length) (1,5). Thus, one PRF schedule maximized the number of N-R transitions, i.e., had a maximum N-length of one, whereas the second PRF schedule had an N-length of four.

EXPERIMENT 1

METHOD

Subjects

Thirty-two male Wistar rats, approximately 4 months old, were housed 4 to a cage under reversed cycle lighting. They received food for 1 hr each day in the home cage, with water freely available.

Apparatus

Four Campden Instruments operant chambers with two retractable levers were used. The right-hand lever was in the retracted position throughout the experiment. The 2.8-W houselight was mounted in the roof of the chamber and was lit throughout the experimental session. The boxes were equipped with pellet dispensers which delivered one 45-mg Campden Instruments food pellet as reinforcement to the

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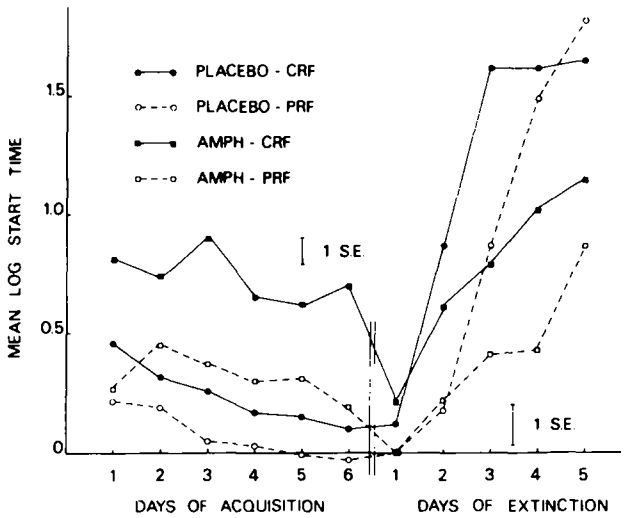

FIG. 1. The course of acquisition and extinction, expressed as mean log Start time, for continuously reinforced (CRF) and partially reinforced (PRF) animals in the placebo and amphetamine (AMPH) conditions. The bars on the left hand and the right hand sides represent one standard error derived from the error term of the ANOVA.

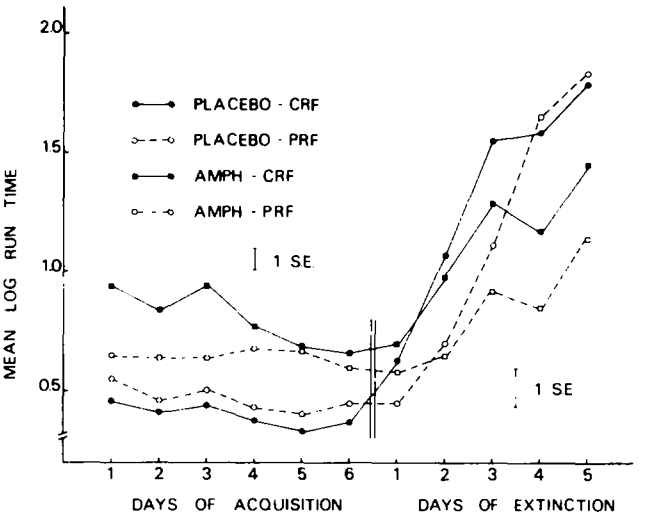

FIG. 2. The course of acquisition and extinction, expressed as mean log Run time, for continuously reinforced (CRF) and partially reinforced (PRF) animals in the placebo and amphetamine (AMPH) conditions. The bars on the left hand and the right hand sides represent one standard error derived from the error term of the ANOVA.

food tray, which was illuminated following animals' response. Entrance to the food tray was by pushing a Perspex panel, hinged at the top. Movements of the panel were monitored with the aid of a microswitch. Equipment programming and data recording were controlled by a microVax microcomputer.

Procedure

All animals received several days of pretraining. For the first two days rats were given 15-min sessions during which the lever was retracted and food pellets were delivered on a variable time (VT) 30-sec schedule. From the third day of pretraining the lever was introduced into the box and two reinforcement schedules were in effect: food was delivered independently of animals' responding on a VT 30-sec schedule, and a continuous reinforcement (CRF) schedule was superimposed on the VT schedule. The free food schedule was discontinued after 10 bar presses. Following five additional bar presses, the CRF schedule was discontinued, and the animals were placed on a progressive fixed ratio (FR) schedule, starting at FR-2 and incrementing by one after every five reinforcements until FR-5 was reached or 30 min elapsed. The lever was available in the box throughout the session. Following 10 reinforcements on FR-5, pretraining was completed. The acquisition stage was initiated the next day and lasted 6 days. Each daily session consisted of 10 discrete trials with an intertrial interval (ITI) of 60 sec. At the start of each trial the retractable lever was inserted into the box. Following five lever presses the tray light came on. As the rat made a tray entry the lever was retracted, and if scheduled, reward was delivered. As the rat made a tray exit, the tray light came off. The continuous reinforcement (CRF) animals received a reward on each of the 10 trials. The partial reinforcement (PRF) subjects received a reward on a quasi-random 50% schedule, i.e., 5 reinforced and 5 nonreinforced trials. Following acquisition, 5 days of extinction commenced. The procedure during extinction was identical to that of acquisition except that no rewards were delivered on any of the trials.

Three time measurements were recorded for each trial: Start time—the time between the insertion of the lever into the box and the first lever press; Run time—the time from the first press to the fifth; and, Goal time—the time between the last press and tray entry. The procedure was programmed such that a maximum duration of 60 sec was allowed for each of the Start, Run and Goal times. If any of these times reached 60 sec, the lever was retracted and the trial terminated. A score of 60 sec was given for each uncompleted segment. A logarithmic transformation was carried out on the start, run and goal times to allow the use of analysis of variance. Separate analyses were performed on the acquisition and extinction data. Both analyses included main factors of drug and reinforcement and a repeated measurements factor of days (6 for acquisition and 6 for extinction). The analysis of the extinction data included the last day of acquisition.

Drug Injections

In pretraining, all animals received saline (0.3 ml) injections 15 min prior to each daily session. In acquisition and extinction, the appropriate drug, 1 mg/kg d-amphetamine sulfate, dissolved in 1 ml of saline, or an equivalent volume of saline, was injected 15 min prior to each daily session.

The subjects were divided into 4 groups in a 2×2 design consisting of drug (amphetamine or placebo) and reinforcement (CRF or PRF). One subject (Amph-PRF) failed to lever press and was excluded from the experiment. Thus, the final group sizes were: Placebo-CRF, n=8; placebo-PRF, n=8; amph-CRF, n=8, and amph-PRF, n=7.

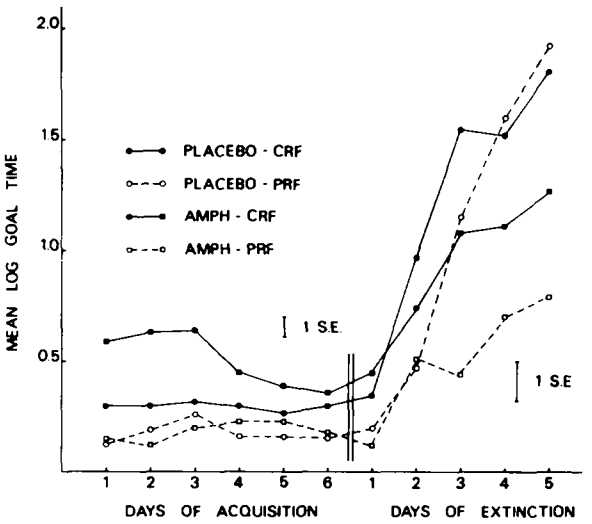

FIG. 3. The course of acquisition and extinction, expressed as mean log Goal time, for continuously reinforced (CRF) and partially reinforced (PRF) animals in the placebo and amphetamine (AMPH) conditions. The bars on the left hand and the right hand sides represent one standard error derived from the error term of the ANOVA.

RESULTS

The results for acquisition and extinction, expressed as mean log Start, Run and Goal times, are presented in Figs. 1, 2 and 3, respectively.

Acquisition

As can be seen in Fig. 1, left side, the administration of amphetamine produced longer start times (longer latency to respond) irrespective of the reinforcement condition. This was supported by the significant main effect of Drug, $F(1,27)=22.67$, $p<0.001$. The same outcome emerged in the Run times (longer time to complete five bar-presses) (see Fig. 2, left side), and was supported by the significant main effect of Drug, $F(1,27)=15.44$, $p<0.001$.

In addition, PRF led to faster Start times compared with CRF. This was supported by the significant main effect of Reinforcement, $F(1,27)=14.67$, $p<0.001$. A similar outcome was obtained for Goal times (see Fig. 3) and was supported by the significant main effect of Reinforcement, $F(1,27)=9.79$, $p<0.005$. In addition, inspection of Fig. 3 reveals that in the Goal, Amph-CRF animals tended to be slower than placebo-CRF animals while the two PRF groups resembled each other in their speeds. This was reflected in the Drug × Reinforcement × Days interaction which approached significance, $F(5,135)=1.89$, $p<0.10$.

Extinction

As can be seen in Figs. 1, 2 and 3 (right side), a clear PREE, i.e., faster Start, Run and Goal times of PRF as compared to CRF animals, was evident in both the Placebo and Amphetamine conditions. This was supported in the Start by the significant main effect of Reinforcement, $F(1,27)=23.25$, $p<0.001$, and the significant Reinforcement × Days interaction, $F(5,135)=2.58$, $p<0.03$; in the Run by the significant main effect of Reinforcement $F(1,27)=7.76$, $p<0.01$, and a significant Reinforcement × Days interaction, $F(5,135)=3.07$, $p<0.02$; and in the Goal by a significant main effect of Reinforcement, $F(1,27)=11.29$, $p<0.003$.

In all three time measurements (see Figs. 1, 2 and 3), amphetamine produced shorter times, i.e., increased resistance to extinction. This was supported in the Start by the significant main effect of Drug, $F(1,27)=20.12$, $p<0.001$, and by the significant Drug × Days interaction, $F(5,135)=18.08$, $p<0.001$; in the Run by the significant main effect of Drug, $F(1,27)=6.98$, $p<0.02$, and by the significant Drug × Days interaction, $F(5,135)=13.77$, $p<0.001$; and in the Goal by the significant main effect of Drug, $F(1,27)=19.53$, $p<0.001$, and the significant Drug × Days interaction, $F(5,135)=10.11$, $p<0.001$. In addition, it can be seen in Figs. 1 and 2 that whereas on days 1, 2 and 3 of extinction, amphetamine led to a comparable increase in resistance to extinction in the CRF and PRF conditions, on days 4 and 5 of extinction the drug led to a more pronounced increase in resistance to extinction in the PRF condition (compare Amph-PRF with Placebo-PRF) than in the CRF condition (compare Amph-CRF with Placebo-CRF). The latter result was supported in the Start by the significant interaction of Drug × Reinforcement × Days, $F(5,135)=2.27$, $p=0.05$, and in the Run by the same interaction which approached significance, $F(5,135)=2.11$, $p<0.07$.

EXPERIMENT 2

METHOD

Subjects

Fifty-four male Wistar rats as in Experiment 1.

Apparatus

As in Experiment 1.

Procedure

Pretraining, acquisition and extinction were carried out exactly as in Experiment 1 but in acquisition, in addition to the CRF schedule, two 40% partial reinforcement schedules were employed: PRF-N-R and PRF-N-length. The PRF-N-R schedule consisted of the following sequences: Day 1:RRNRNRNRNR; Day 2: RNRNRNRNRR; Day 3: NRNRNRNRRR; Days 4, 5 and 6 of acquisition were identical to days 1, 2, and 3, respectively. The PRF-N-length schedule consisted of the following sequences: Day 1: RRRRNNNNRR; Day 2: RRRNNNNRRR; Day 3: RRNNNNRRRR; Days 4, 5 and 6 were identical to days 1, 2 and 3, respectively.

The animals were divided into six groups in a 2×3 design consisting of drug (amphetamine, placebo) and reinforcement schedule (CRF, N-R, and N-length). Two subjects (one Amph-CRF and one Placebo-CRF) failed to bar press and were excluded from the experiment. Thus, the final group sizes were: Placebo-CRF, n=8; Placebo PRF-N-R, n=9; Placebo PRF-N length, n=9; Amphetamine CRF, n=8; Amphetamine PRF-N-R, n=9; Amphetamine-PRF-N length, n=9.

Data collection and analyses, as well as drug injections, were identical to Experiment 1.

RESULTS

The results of acquisition and extinction, expressed as

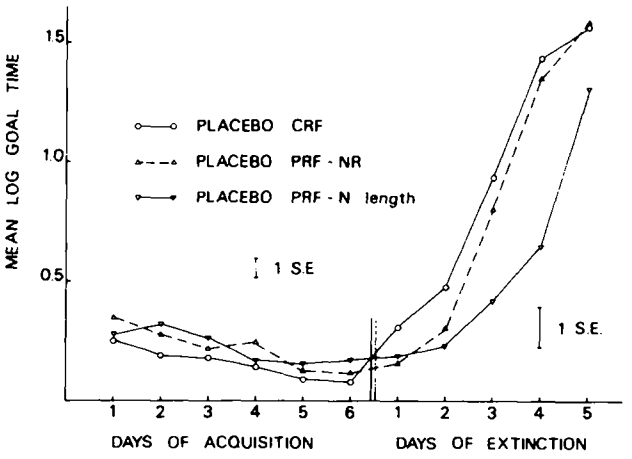

FIG. 4. The course of acquisition and extinction, expressed as mean log Goal time for the placebo groups trained on CRF, N-R and N-length schedules. The bars on the left hand and the right hand sides represent one standard error derived from the error term of the ANOVA.

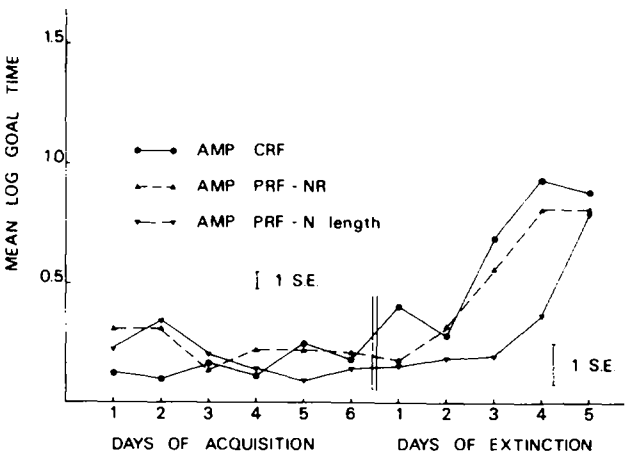

FIG. 5. The course of acquisition and extinction, expresses as mean log Goal time for the amphetamine (AMP) groups trained on CRF, N-R and N-length schedules. The bars on the left hand and the right hand sides represent one standard error derived from the error term of the ANOVA.

mean log Goal times for the Placebo and Amphetamine conditions, are presented in Figs. 4 and 5, respectively. These results are representative of the log Start and Run results.

Acquisition

As can be seen in Figs. 4 and 5 (left side), CRF animals were faster than the N-R and N-length animals on the first two days of acquisition. This was supported by the significant Reinforcement × Days interaction, $F(10,230)=1.92$, $p<0.05$. In addition, amphetamine-treated animals tended to have shorter Goal times at the beginning of acquisition and slightly longer times towards the end of acquisition. This was reflected in the Drug × Days interaction which approached significance, $F(5,230)=2.17$, $p<0.06$. No significant main effects or interactions were found in the analyses of log Start and Run times.

Extinction

As can be seen in Figs. 4 and 5 (right side), in both the Amphetamine and Placebo conditions, only the PRF-N-length schedule led to faster log Goal times, i.e., increased resistance to extinction in comparison to the CRF schedule. There was no indication of increased resistance to extinction in animals trained on the PRF-N-R schedule. The presence of the PREE in the PRF-N length group was supported in the analysis of the log Goal times by the significant main effect of Reinforcement, $F(2,46)=3.30$, $p<0.05$, and by the significant Reinforcement × Days interaction, $F(10,230)=2.91$, $p<0.005$. An identical outcome emerged in the analyses of the log Start and log Run times. The analysis of log Start times yielded a significant main effect of Reinforcement, $F(2,46)=6.72$, $p<0.005$, and a significant Reinforcement × Days interaction, $F(10,230)=4.59$, $p<0.001$. In the Run, there was a significant main effect of Reinforcement, $F(2,46)=8.64$, $p<0.001$, and a significant Reinforcement × Days interaction, $F(10,230)=3.17$, $p<0.001$.

The administration of amphetamine resulted in increased resistance to extinction (shorter times) irrespective of reinforcement schedule. This was supported in the Goal by the significant main effect of Drug, $F(1,46)=5.86$, $p<0.02$, and by the significant Drug × Days interaction, $F(5,230)=8.13$, $p<0.001$. The same results were obtained in the analyses of log Start and log Run times. In the Start, this was supported by the significant main effect of Drug, $F(1,46)=8.66$, $p<0.01$, and by the significant Drug × Days interaction, $F(5,230)=14.53$, $p<0.001$; in the Run, by the significant Drug × Days interaction, $F(5,230)=11.83$, $p<0.001$. It should be pointed out that the analyses of the log Start, Run and Goal times yielded no significant Drug × Reinforcement interactions.

DISCUSSION

In both experiments, amphetamine-treated animals exhibited a normal PREE under the conditions in which no-drug animals showed the PREE, i.e., random 50% partial reinforcement and N-length schedules. This result is in line with our previous finding that the drug did not disrupt a multitrial PREE in the runway (2). When an N-R schedule was used, both drug and no-drug animals did not show the PREE. These results demonstrate that the processes underlying the development of resistance to extinction at short ITI's are not affected by amphetamine.

Increased resistance to extinction at short ITI's is believed to be primarily mediated by memory traces of nonreinforcement (3,5) as postulated by Capaldi (1). According to this view, higher resistance to extinction exhibited by PRF animals is due to the fact that these animals are reinforced for responding in the presence of memory traces of nonreinforcement (NR). In other words, on reinforced trials, an association is formed between the outcome of preceding trials (memory traces of NR) and the outcome of subsequent trials (reinforced response). Evidently, this process is not affected by amphetamine, as attested by the presence of PREE in amphetamine-treated animals in both the operant chamber and in the runway (2). As for the absence of the PREE in the N-R condition, Mackintosh (5) suggested that the disappearance of increased resistance to extinction on

N-R schedules is due to the fact that on such schedules animals learn to discriminate/anticipate the occurrence of reinforcement and nonreinforcement. The fact that amphetamine-treated animals trained on N-R schedule did not show the PREE, indicates that also such a discriminative capacity is intact under the drug.

In summary, the present experiments demonstrate that on a PRF schedule with short ITI's, amphetamine-treated animals are not impaired in their capacity to learn sequences of events and to associate the outcomes of preceding trials with subsequent consequences. It is important to emphasize that the same outcome is produced in different types of apparatus, (operant chamber and runway) which differ in the type of responses the animal is required to make and the nature of the controlling stimuli (5). In contrast, at least in the runway, amphetamine was found to disrupt the PREE at a 24 hr ITI (7,8). The development of the 1 trial/day PREE is believed to be underlied by a different learning process from that of the multitrial PREE (3,5), and we suggested that the differential effects of amphetamine on the two kinds of PREE are determined by the type of learning process involved in the two phenomena (2).

The administration of amphetamine did yield an outcome not obtained in the runway, namely, a general increase in resistance to extinction in both the PRF and the CRF animals. The fact that this effect was independent of the reinforcement schedule suggests that it is not related to the processes underlying the development of PREE. One possibility is that the increased resistance to extinction reflected the well known amphetamine-induced response perseveration (4), which would not be expected to develop in a runway procedure that involves a single running response per trial and a much longer interval (at least 5 min) among responses. Another possibility is that the tray light served as a more effective conditioned reinforcement for amphetamine-treated animals, since this drug is known to enhance the effectiveness of conditioned reinforcers (6).

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REFERENCES

1. Capaldi, E. J. A sequential hypothesis of instrumental learning. In: Spence, K. W.; Spence, J. T., eds. The psychology of learning and motivation. vol. 1. New York: Academic Press; 1967:67–156.
2. Feldon, J.; Bercovitz, H.; Weiner, I. The effects of amphetamine on a multitrial partial reinforcement extinction effect (PREE) in the runway. Pharmacol. Biochem. Behav. 32:55–63; 1988.
3. Gray, J. A. Elements of a two-process theory of learning. London: Academic Press; 1975.
4. Lyon, M.; Robbins, T. W. The action of central nervous system stimulant drugs: A general theory concerning amphetamine effects. In: Essman, W. B.; Valzelli, L., eds. Current developments in psychopharmacology. vol. 2. New York: Spectrum; 1975:79–163.
5. Mackintosh, N. J. The psychology of animal learning. London: Academic Press; 1974.
6. Taylor, J. R.; Robbins, T. W. Enhanced behavioural control by conditioned reinforcers following microinjections of d-amphetamine into the nucleus accumbens. Psychopharmacology (Berlin) 84:405–412; 1984.
7. Weiner, I.; Bercovitz, H.; Lubow, R. E. Feldon, J. The abolition of the partial reinforcement extinction effect by amphetamine. Psychopharmacology (Berlin) 86:318–323; 1985.
8. Weiner, I.; Feldon, J.; Bercovitz, H. The abolition of the partial reinforcement extinction effect (PREE) by amphetamine: Disruption of control by nonreinforcement. Pharmacol. Biochem. Behav. 27:205–210; 1987.