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The Effects of Amphetamine on a Multitrial Partial Reinforcement Extinction Effect (PREE) in a Runway

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FELDON, J., H. BERCOVITZ AND I. WEINER. *The effects of amphetamine on a multitrial partial reinforcement extinction effect (PREE) in a runway.* PHARMACOL BIOCHEM BEHAV 32(1) 55–63, 1989.—Three experiments examined the effects of d-amphetamine (1 mg/kg) administration on the partial reinforcement extinction effect (PREE) using a multitrial procedure. Two groups of rats were trained to run in a straight alley. The continuously reinforced (CRF) group received food reward on every trial. The partially reinforced (PRF) group was rewarded on a quasi-random 50% schedule. All animals were then tested in extinction. Experiments 1 and 2 used 6 trials/day with an intertrial interval (ITI) of 5 min. In Experiment 1 the drug was administered only during acquisition, whereas in Experiment 2 it was administered throughout acquisition and extinction. Experiment 3 used 3 trials/day with a 20 min ITI. The drug was administered throughout acquisition and extinction. In all three experiments, amphetamine-treated animals showed a normal PREE, i.e., increased resistance to extinction in PRF as compared to CRF animals. These results stand in marked contrast to the amphetamine-induced abolition of the PREE with 1 trial/day procedure.

d-Amphetamine Continuous reinforcement Partial reinforcement Intertrial interval Resistance to extinction Rat

THE partial reinforcement extinction effect (PREE) refers to the finding that animals trained on a partial reinforcement (PRF) schedule show increased resistance to extinction as compared to continuously reinforced animals (17). We showed that the PREE was abolished by amphetamine (19,20). This abolition was entirely due to decreased resistance to extinction of the drug-injected PRF animals, while the performance of the drug-injected CRF controls was unaffected. Increased resistance to extinction produced by partial as compared to continuous reinforcement is assumed to reflect the fact that PRF animals learn to respond in the presence of stimuli produced on nonreinforced trials (7,17). Thus, our results indicated that amphetamine disrupts the behavioral control of stimuli associated with nonreinforcement. In further support of this conclusion, we showed that the PREE was abolished by the administration of amphetamine to PRF animals on nonreinforced trials only, irrespective of drug treatment (amphetamine or saline) on reinforced trials (20).

The above PREE experiments used a 1 trial/day procedure, i.e., acquisition and extinction trials were given with a 24-hr intertrial interval (ITI). The present experiments sought to test whether amphetamine would abolish the PREE when shorter ITI's are used (a multitrial procedure). It is well documented that the development of resistance to extinction at short and long ITI's is governed by different processes (7–11, 17). Thus, PREE at short and long ITI's is differentially affected by various parameters of the training schedule such as the number of transitions between reinforced and nonreinforced trials, the number of nonreinforced trials preceding a given reinforced trial (N-length) or the absolute number of nonreinforced trials (17) as well as by drugs, such as anxiolytics (6,10). The most accepted explanation for these differences is that control by stimuli associated with nonreinforcement is acquired at short and long ITI's via different learning processes (7, 11, 17). With long ITI's, nonreinforcement-elicited stimuli are conditioned to the apparatus cues, which are then associated with reinforcement on the following trials. At short ITI's, nonreinforcement-elicited stimuli are associated directly with reinforcement on reinforced trials. The question addressed in the present experiments was whether also under the latter conditions amphetamine would disrupt the behavioral control of stimuli associated with nonreinforcement.

Experiments 1 and 2 used 6 trials/day with a 5-min ITI and Experiment 3 used 3 trials/day with a 20-min ITI. In Experi-

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ment 1, amphetamine was administered during acquisition only, since in our earlier experiment (19) PREE was abolished by drug administration in acquisition independently of drug treatment (amphetamine or saline) in extinction. Since in Experiment 1 this treatment left the PREE intact, we tested in Experiment 2 whether the same result would be obtained when the drug was administered throughout acquisition and extinction. Also in this experiment, amphetamine-treated animals showed a normal PREE. Consequently, in Experiment 3, we lengthened the ITI to 20 min in order to determine whether also with a longer ITI, amphetamine would not affect the PREE in a multitrial procedure.

EXPERIMENT 1

METHOD

Subjects

The subjects were 40 male Wistar rats (Tel-Aviv University Medical School, Israel) approximately 4 months old. Throughout the experiment, they were fed for 1 hr a day, commencing at least 1 hr after the last animal had been run that day. Water was freely available.

Apparatus

The apparatus consisted of a straight alley made out of transparent perspex with black rubber curtains covering the sides. The runway was 140 cm long, 15 cm wide and 35 cm high, with a startbox (20 cm long) and a goalbox (20 cm long) separated by a run section (100 cm long). The floor consisted of a metal grid composed of equally spaced rods. The startbox door was made of transparent Plexiglas and opened vertically downwards. The door was operated by a solenoid controlled by a pushbutton. The goalbox door was of metal and could be raised and lowered manually. The food pellets were placed in a recessed compartment 4 cm wide and 2.5 cm deep at the far side of the goalbox. There were three light photobeams and photocells, the first one 2 cm beyond the startbox, the second 2 cm before the goal section and the third inside the goalbox. The latter was interrupted when the rat contacted the food compartment. The photobeams operated three electronic timers, accurate to 0.01 sec. The first timer timed the start section (from the opening of the start door to the first photobeam); the second timed the run section (from the first to the second photobeam) and the third, the goal section (from the second to the third photobeam). Prior to each trial, the goalbox door was raised and, on rewarded trials, food was manually placed in the food compartment. Each reward consisted of four 45-mg Campden Instruments food pellets. Once the animal interrupted the goalbox photobeam, the goalbox door was lowered. A Rockwell-AIM 65 microprocessor was used for equipment programming and data recordings.

Procedure

Animals were put on food deprivation one week prior to the beginning of the experiment. They were then handled for 2 weeks and given 2 days of pretraining. On day 1 of pretraining, animals were introduced into the alley in groups of four for 20 min. All alley doors were open and food pellets were available in the goalbox compartment. On the second day, animals were placed in the alley in pairs for 10 min, again with food pellets available. The experimenter ensured that all animals reached the goalbox and ate from the food compartment. On the third day, the acquisition stage, consisting of 7 days, began. On each day, each subject was run for 6 trials per day, with a 5-min intertrial interval. On each trial, the animal was placed in the start section and the three time measurements for the start, run and goal sections were recorded. The CRF subjects received a reward on every trial. The PRF animals were rewarded on a quasi-random 50% schedule, i.e., three reinforced and three nonreinforced trials on each day, according to the following schedule: Day 1—NRNRNR; Day 2—NRNNRR; Day 3—NNRRNR; Day 4—RNRNNR; Day 5—RNNRNR; Day 6—NNRNRR; Day 7—NRRNNR, where R is a rewarded trial and N is a nonrewarded trial. Following acquisition, animals were given 4 days rest in their home cages. At the end of the rest period, all animals were given 2 days of CRF retraining as in acquisition. The rest period and CRF retraining were modelled after Weiner *et al.* (20) and served to prevent performance deficits in extinction resulting from the switch from drug in acquisition to placebo in extinction. Following retraining, 4 days of extinction were given. In extinction, animals were run exactly as in acquisition but no rewards were given. Any subject failing to move from one section of the alley to the other within 100 sec was removed from the apparatus and returned to its homecage. After two consecutive 100-sec trials in one session, the animal was dropped from the experiment and given a score of 100 sec for all sections of the runway on all subsequent extinction trials.

The rats were randomly assigned to four experimental groups in a 2×2 design, consisting of drug-no drug in acquisition and reinforcement schedule (CRF, PRF). Six subjects (three from the Amphetamine-CRF group, 2 from Placebo-PRF group, and one from the Amphetamine-PRF group) failed to acquire the running response and were excluded from the experiment. Thus, the final analysis was performed on 34 subjects: Amphetamine-CRF, n=7; Amphetamine-PRF, n=9; Placebo-CRF, n=10; Placebo-PRF, n=8.

Drug Injections

The appropriate drug, either 1 mg/kg d-amphetamine sulfate dissolved in 1 ml saline, or an equivalent volume of saline, was given IP 15 min prior to the daily session during acquisition. Retraining and extinction were carried out without drugs.

Data Analysis

The data were transformed into reciprocals to allow the use of analysis of variance. Separate ANOVAs were performed for each of the stages. For each stage, start, run and goal data were analyzed separately. The analyses of the three stages included two main factors of drug and reinforcement schedule in acquisition and a repeated measurements factor of days. The analyses of extinction included the last day of retraining. Since at the end of retraining animals in the different conditions reached slightly different asymptotic levels of performance, which could affect the interpretation of the extinction results, an Anderson transformation (3) was applied to the extinction data. This transformation takes into account in the analysis of the extinction data the individual speeds of the animals at the end of the preceding stage and thus transforms extinction speed scores into rate scores, thereby eliminating distortions in the interpretation of the extinction results which may stem from the different running speeds at the end of the preceding stage. The

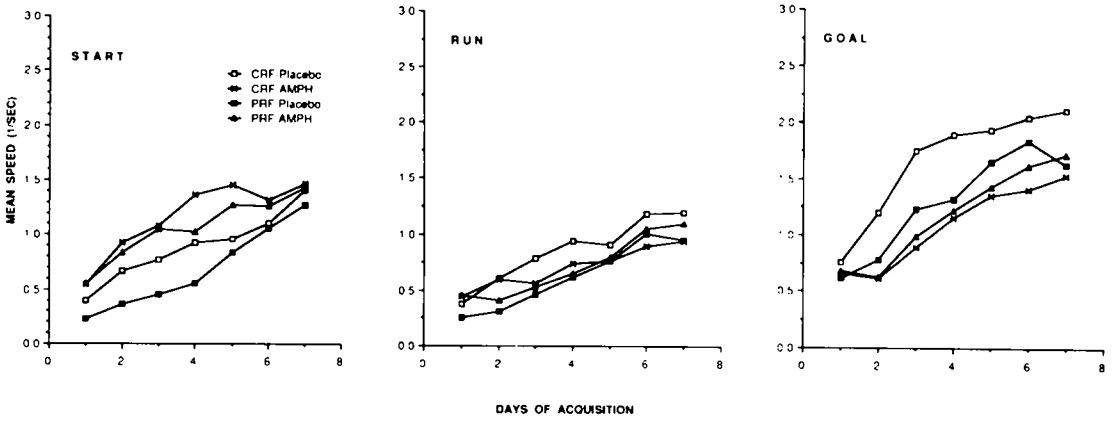

FIG. 1. The course of acquisition expressed as means of six daily trials in the Start (left panel), Run (middle panel) and Goal (right panel) sections as a function of acquisition reinforcement schedule (continuous, CRF, or partial, PRF, reinforcement) and drug condition (1 mg/kg d-amphetamine, AMPH, or placebo).

transformation is arrived at using the formula: f(n) = [R (∞) − R (n)]/[R (∞) − R (1)], where f(n) is the transformed score, R (n) is the speed of the subject on trial n, R (1) is the speed on the last trial of the preceding stage, and R (∞) is the speed on the last trial of extinction. Thus, for the extinction data, we report the results of the analysis of the extinction speeds as well as an analysis of the rate of extinction (Anderson transformation).

RESULTS

Acquisition

Figure 1 presents mean running speeds (1/sec) of the four groups in the three sections of the alley: start, run and goal. As can be seen, amphetamine administration produced different effects in the three sections of the alley.

In the Start section, the drug led to shorter latencies of leaving the startbox irrespective of the reinforcement schedule. This was supported by the significant main effect of Drug, $F(1,30)=12.07$, $p<0.002$, and by the significant Drug × Days interaction, $F(6,180)=3.95$, $p<0.001$. In the Run, amphetamine-treated animals were faster at the beginning of acquisition and slower at the end of acquisition. This was supported by the Drug × Days interaction which approached significance, $F(6,180)=2.11$, $p<0.06$. In the Goal, amphetamine led to slower running speeds, as reflected in the significant main effect of Drug, $F(1,30)=9.15$, $p<0.005$, and in the significant Drug × Days interaction, $F(6,180)=2.65$, $p<0.02$. In addition, in the Run section, CRF groups tended to be faster than the PRF groups, particularly at the early stages of acquisition. This was supported by the significant Reinforcement × Days interaction, $F(6,180)=2.25$, $p<0.05$. In the Goal section, reinforcement schedule affected differently the Amphetamine and Placebo animals: in the Placebo animals, the PRF group was noticeably slower than the CRF group, whereas in the amphetamine-treated animals, the PRF group was slightly faster than the CRF group. This was supported by the significant Drug × Reinforcement interaction, $F(1,30)=4.28$, $p<0.05$.

Retraining

Figure 2 (panel A) presents the results for the retraining stage, expressed in mean running speeds (1/sec) in the Run section of the alley. As can be seen (Fig. 2, panel A), amphetamine administration in acquisition led to slower running speeds in retraining. This was supported by the significant main effect of Drug, $F(1,30)=4.79$, $p<0.04$. A similar outcome was obtained in the Goal section, and was supported by the significant main effect of Drug, $F(1,30)=8.06$, $p<0.01$.

Extinction

The analysis of the extinction data yielded similar results across the Start, Run and Goal sections of the alley, unlike those obtained in the acquisition. Figure 2 (panels B and C) depicts extinction performance in the Run section, which is representative of the results in the Start and Goal sections, expressed as mean running speeds (1/sec) (panel B) as well as means of the extinction scores following Anderson transformation (panel C). As can be seen (Fig. 2, panel B), a clear PREE, i.e., faster running speeds of the PRF as compared to CRF animals, was obtained in both the Placebo and the Amphetamine conditions. The presence of the PREE was supported in the Run by the significant main effect of Reinforcement, $F(1,30)=6.62$, $p<0.02$, and by the Reinforcement × Days interaction which approached significance, $F(4,120)=2.38$, $p<0.06$; in the Goal, by the significant main effect of Reinforcement, $F(1,30)=10.14$, $p<0.005$, and by the significant Reinforcement × Days interaction, $F(4,120)=7.28$, $p<0.001$. In addition, as can be seen in Fig. 2 (panel B), a decrease in resistance to extinction, i.e., slower running speeds, was evident in amphetamine-treated animals. This was supported in the Run and Goal sections by the significant main effects of Drug, $F(1,30)=4.42$, $p<0.05$, and, $F(1,30)=9.14$, $p<0.005$, respectively. This tendency was reduced but remained significant when the statistical analysis was performed on the rate of extinction using an Anderson transformation (see Fig. 2, panel C). In the Run, this was supported by the significant main effect of Drug, $F(1,30)=4.42$, $p<0.05$, and in the Goal by a main effect of Drug which approached significance, $F(1,30)=4.05$, $p<0.06$, and by the significant Drug × Days interaction, $F(4,120)=3.93$, $p<0.05$. Likewise, the PREE was evident following an Anderson transformation both in the Run and in the Goal sections, as reflected in the

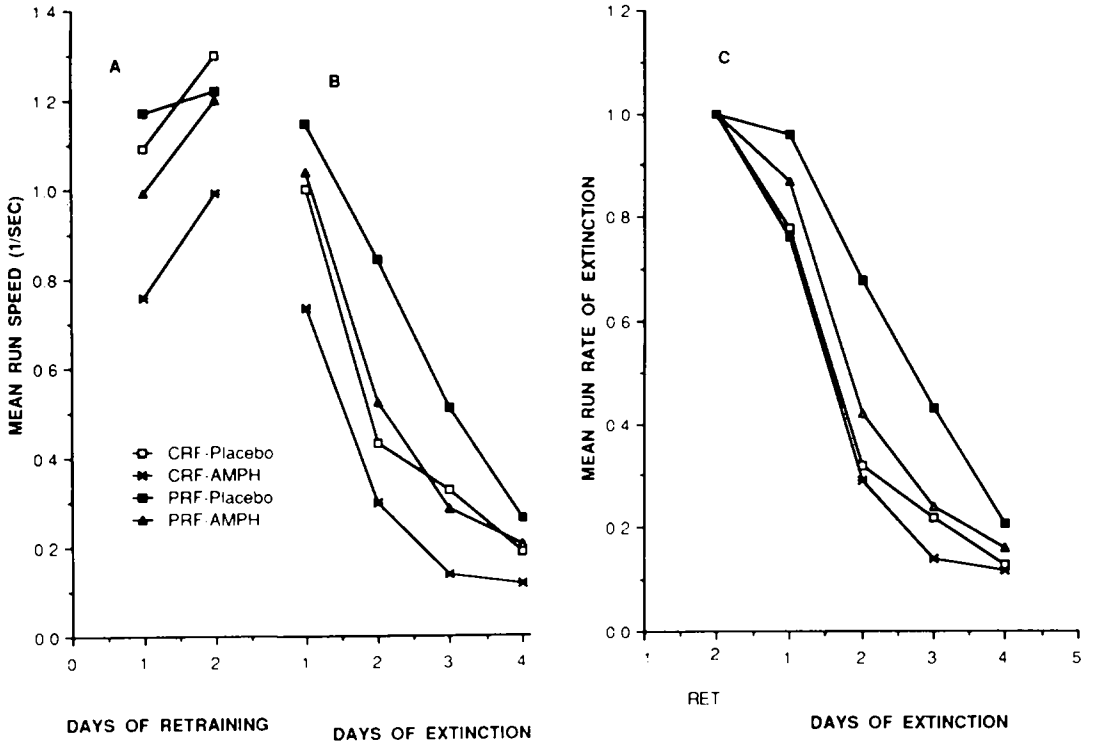

FIG. 2. The course of retraining (panel A) and extinction (panel B) expressed as means of six daily trials in the Run section as a function of acquisition reinforcement schedule (CRF or PRF) and drug condition (amphetamine, AMPH, or placebo). Panel C presents the extinction data following an Anderson (3) transformation which yields a rate measure.

significant main effect of Reinforcement in the Run, $F(1,30)=11.80$, $p<0.002$, and in the Goal, $F(1,30)=22.03$, $p<0.001$, as well as by the significant Reinforcement × Days interactions in the Run, $F(4,120)=3.75$, $p<0.01$, and in the Goal, $F(4,120)=7.96$, $p<0.001$.

EXPERIMENT 2

Subjects

The subjects were 28 male Wistar rats as in Experiment 1.

Apparatus

As in Experiment 1.

Procedure

The procedure was identical to that of Experiment 1 except for the following changes: 1) Acquisition stage lasted 8 days. The PRF schedule on day 8 was: RRNNNR. 2) Extinction was given immediately following acquisition, and lasted 6 days.

The rats were randomly assigned to four experimental groups in a 2×2 design consisting of drug-no drug in acquisition and extinction and reinforcement schedule (CRF, PRF).

Drug Injections

One mg/kg d-amphetamine or saline (as in Experiment 1) were administered throughout acquisition and extinction.

Data Analysis

As in Experiment 1. The analysis of extinction included the last day of acquisition.

RESULTS

Acquisition

The results, expressed in mean running speeds (1/sec), in the Start, Run and Goal sections, are presented in Fig. 3.

As can be seen, the administration of amphetamine exerted different effects in the three alley sections in the CRF and PRF conditions. In the Start, placebo PRF group was faster than placebo-CRF group, while amphetamine-PRF group was slower than amphetamine-CRF group. This outcome was supported by the significant interaction of Drug × Reinforcement, $F(1,24)=10.40$, $p<0.005$, and by the significant interaction of these factors with Days, $F(7,168)=2.73$, $p<0.01$. In the Run, CRF and PRF placebo animals exhibited similar running speeds; in the amphetamine animals, the CRF group was faster than the two placebo groups, but the PRF group was slower than the two placebo groups. This was supported by the significant Drug × Reinforcement interaction, $F(1,24)=6.74$, $p<0.02$. In the Goal, amphetamine tended to decrease speeds, irrespective of the reinforcement schedule, and this was reflected in the main effect of Drug which approached significance, $F(1,24)=3.69$, $p<0.07$. In addition, the PRF groups were slower than the CRF groups, irrespective of the drug condi-

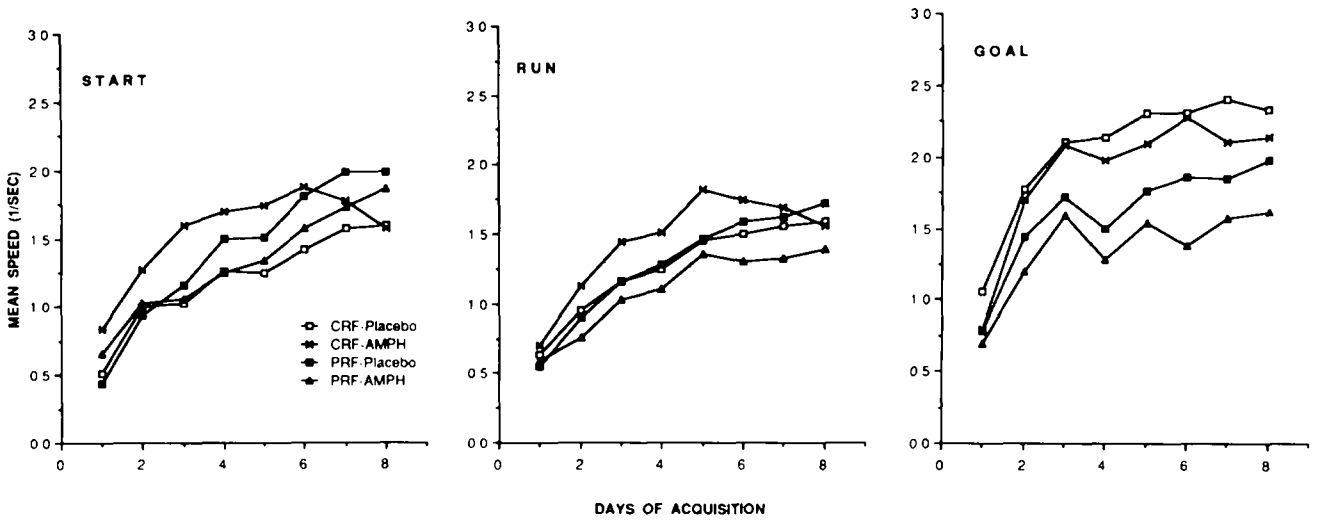

FIG. 3. The course of acquisition expressed as means of six daily trials in the Start (left panel), Run (middle panel) and Goal (right panel) sections as a function of acquisition reinforcement schedule (continuous, CRF, or partial, PRF, reinforcement) and drug condition (1 mg/kg d-amphetamine, AMPH, or placebo).

tion. This was supported by the significant main effect of Reinforcement, $F(1,24)=20.52$, $p<0.001$, and by the significant Reinforcement × Days interaction, $F(7,168)=3.28$, $p<0.03$.

Extinction

Again, the analysis of the extinction data yielded similar results across the Start, Run and Goal sections. Figure 4 depicts extinction performance in the Run section, expressed as mean running speeds (1/sec) (panel A) as well as means of the extinction scores following Anderson transformation (panel B). These results are representative of those in the Start and Goal sections.

The major outcome of extinction consisted of faster running speeds of the PRF as compared to CRF groups in all sections of the alley, irrespective of the drug treatment. Thus, the PREE was obtained in both the Placebo and Amphetamine animals. The presence of the PREE was supported by the significant main effect of Reinforcement in the three alley sections: Start, $F(1,24)=8.95$, $p<0.006$; Run, $F(1,24)=12.83$, $p<0.001$; Goal, $F(1,24)=5.77$, $p<0.03$. Likewise, the interaction of Reinforcement × Days was significant in the three sections: Start, $F(6,144)=2.51$, $p<0.03$; Run, $F(6,144)=7.85$, $p<0.001$; Goal, $F(6,144)=13.80$, $p<0.001$. In addition, the analysis of the extinction data performed on speeds pointed to decreased resistance to extinction in amphetamine-treated animals (see panel A). This was supported in the Run by the main effect of Drug which approached significance, $F(1,24)=3.46$, $p<0.07$, and in the Goal, by the significant main effect of Drug, $F(1,24)=5.39$, $p<0.003$, and the significant Drug × Days interaction, $F(6,144)=2.45$, $p<0.03$. As can be seen in Fig. 4 (panel B), when Anderson transformation was applied, it became evident that the slower running speeds of the amphetamine animals, as compared to placebo animals, reflected a carry-over effect from acquisition and did not represent a genuine effect of the drug on resistance to extinction. This fact was supported by the complete disappearance of the main effects of Drug following an Anderson transformation in the Run section, $F(1,24)=0.53$, $p>0.5$, and in the Goal section, $F(1,24)=1.82$, $p>0.2$, and by the disappearance of the Drug × Days interaction in the Goal, $F(6,144)=1.69$, $p>0.15$. Unlike the decrement in resistance to extinction, the PREE continued to be evident also in the extinction analyses following Anderson transformation. This was supported in the Run by the significant main effect of Reinforcement, $F(1,24)=25.00$, $p<0.001$, and by the significant Reinforcement × Days interaction, $F(6,144)=7.95$, $p<0.001$, and in the Goal, by the significant main effect of Reinforcement, $F(1,24)=38.5$, $p<0.001$, and by the significant Reinforcement × Days interaction, $F(6,144)=9.60$, $p<0.001$.

EXPERIMENT 3

Subjects

Thirty-six male Wistar rats as in Experiment 1.

Apparatus

As in Experiment 1.

Procedure

The procedure was like that of Experiment 2 with the following changes: 1) In acquisition (8 days) three trials were given per daily session, with an ITI of 20 min. The PRF subjects were reinforced on 50% of the trials according to the following schedule: Day 1—RNR; Day 2—NNR; Day 3—NRR; Day 4—NNR; Day 5—NRR; Day 6—NNR; Day 7—RNR; Day 8—NNR, where R is a rewarded trial and N is a nonrewarded trial. 2) Extinction lasted 8 days. The criterion for extinction was animal's failure to move from one section of the alley to the next within 100 sec on two trials in one session. After two such trials, the animal was dropped from the experiment and given a score of 100 sec for all sections of the alley on all subsequent extinction trials. The

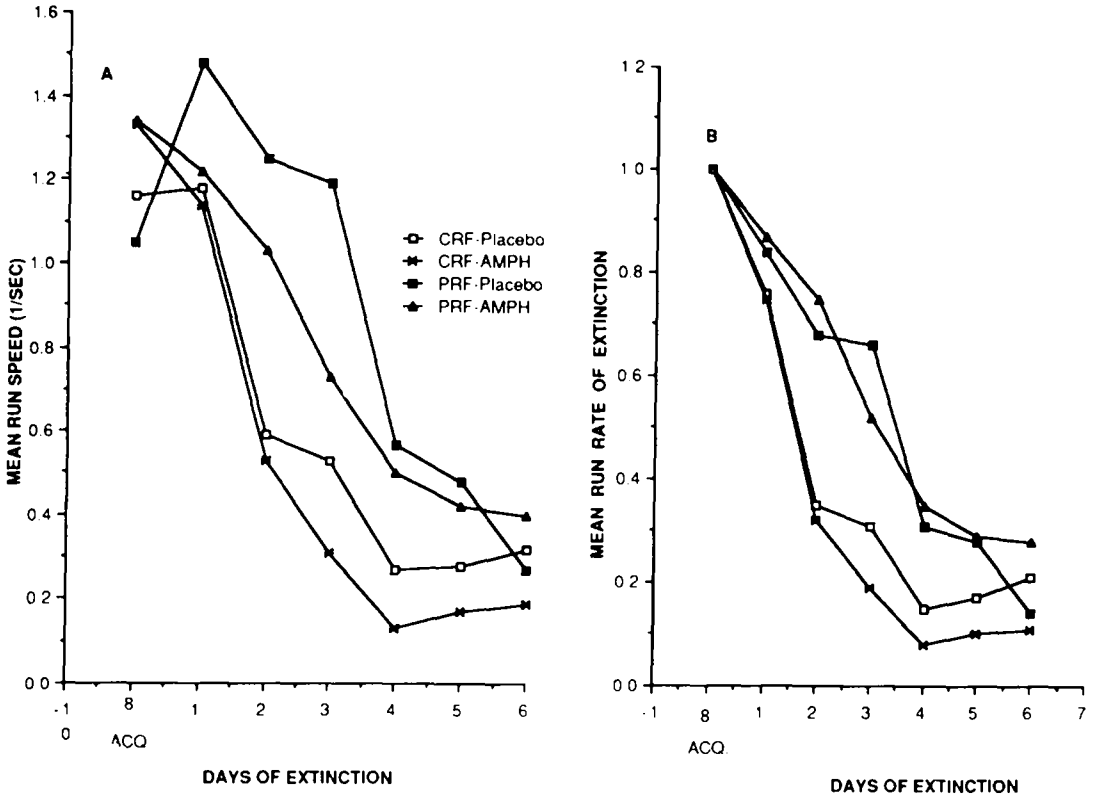

FIG. 4. The course of extinction (panel A) expressed as means of six daily trials in the Run section as a function of acquisition reinforcement schedule (continuous, CRF, or partial, PRF, reinforcement) and drug condition (1 mg/kg d-amphetamine, AMPH, or placebo). Panel B presents the extinction data following an Anderson (3) transformation which yields a rate measure.

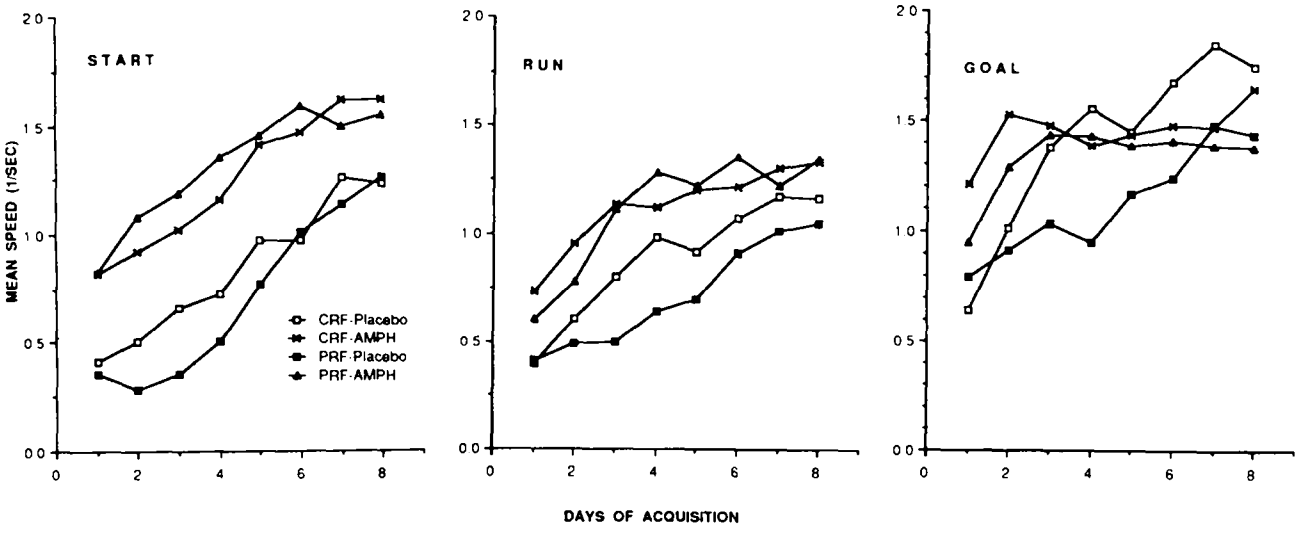

FIG. 5. The course of acquisition expressed as means of three daily trials in the Start (left panel), Run (middle panel) and Goal (right panel) sections as a function of acquisition reinforcement schedule (continuous, CRF, or partial, PRF, reinforcement) and drug condition (1 mg/kg d-amphetamine, AMPH, or placebo).

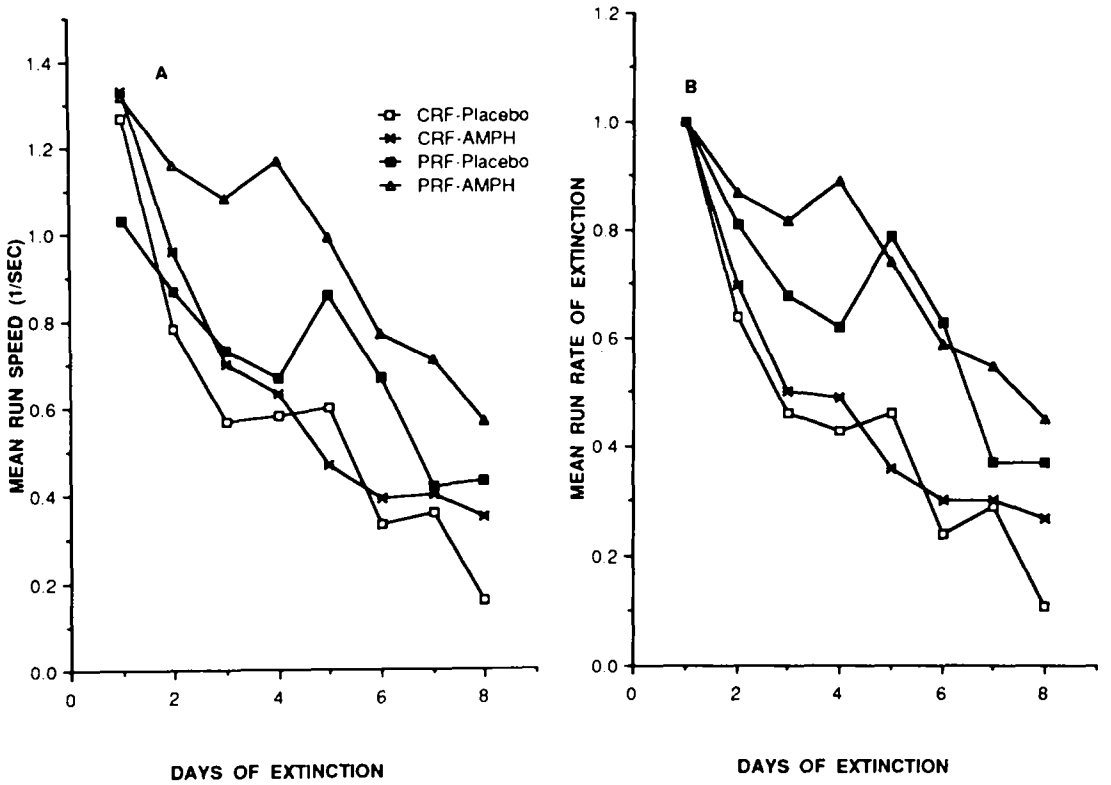

FIG. 6. The course of extinction (panel A) expressed as means of three daily trials in the Run section as a function of acquisition reinforcement schedule (continuous, CRF, or partial, PRF, reinforcement) and drug condition (1 mg/kg d-amphetamine, AMPH, or placebo). Panel B represents the extinction data following an Anderson (3) transformation which yields a rate measure.

rats were randomly assigned to four experimental groups in a 2×2 design consisting of drug-no drug in acquisition and extinction and reinforcement schedule (CRF, PRF). Three subjects (one from Amph-CRF, one from Placebo-PRF and one from Amph-PRF) failed to acquire the running response and were excluded from the experiment. Thus, the final analysis was performed on 33 subjects: Placebo-CRF, n=9; Amph-CRF, n=8; Placebo-PRF, n=8; Amph-PRF, n=8.

Drug Injections

As in Experiment 2, i.e., throughout acquisition and extinction.

Data Analysis

As in Experiment 1.

RESULTS

Acquisition

The results, expressed in mean running speeds (1/sec) in the Start, Run and Goal sections, are presented in Fig. 5.

As can be seen, in the Start and Run sections, amphetamine administration led to faster running speeds in both CRF and PRF conditions. This was supported in the Start by the significant main effect of Drug, $F(1,29)=31.18$, $p<0.001$, and in the Run by the significant main effect of Drug, $F(1,29)=19.93$, $p<0.001$, as well as by the significant Drug × Days interaction, $F(7,203)=3.03$, $p<0.005$. In the Goal, there was an overall tendency for the PRF animals to be slower than the CRF animals, as indicated by the significant main effect of Reinforcement, $F(1,29)=4.93$, $p<0.04$. In addition, in the Goal, there was a tendency for amphetamine animals to be faster at the start of acquisition and slower towards its end. This was supported by the significant Drug × Days interaction, $F(7,203)=4.57$, $p<0.001$.

Finally, as can be seen in Fig. 5, in both the Run and Goal sections, in the placebo condition, the PRF animals tended to be slower than CRF animals. This tendency was completely absent in the Amphetamine condition, in which the CRF and PRF groups showed a highly similar pattern in the acquisition of the running response. The latter result was supported by the significant Drug × Reinforcement × Days interactions in the Run, $F(7,203)=3.19$, $p<0.005$, and in the Goal, $F(7,203)=2.32$, $p<0.03$.

Extinction

Figure 6 depicts extinction performance in the Run section, which is representative of those in the Start and Goal sections, expressed in mean running speeds (1/sec) (panel A) and as means of the extinction scores following an Anderson transformation (panel B).

As can be seen (panel A), PRF animals exhibited faster running speeds than CRF animals. The presence of PREE was supported in the Start by the significant main effect of

Reinforcement, $F(1,29)=12.65$, $p<0.002$, and by the significant Reinforcement × Days interaction, $F(7,203)=4.85$, $p<0.001$; in the Run, by the significant main effect of Reinforcement, $F(1,29)=7.76$, $p<0.01$, and by the significant Reinforcement × Days interaction, $F(7,203)=3.72$, $p<0.001$, and in the Goal, by the significant Reinforcement × Days interaction, $F(7,203)=3.00$, $p<0.005$. In addition, the analysis of running speeds indicated that the administration of amphetamine led in the Start and in the Run (see panel A) sections to an increased resistance to extinction, irrespective of reinforcement conditions. This was supported by the significant main effect of Drug in the Start, $F(1,29)=8.88$, $p<0.01$, and in the Run, $F(1,29)=4.50$, $p<0.04$. However, similarly to Experiment 2, this drug effect was due to faster running speeds of the amphetamine animals as compared to placebo animals in the acquisition stage and did not represent a genuine drug effect on resistance to extinction. This was supported by the complete disappearance of the main effect of Drug following an Anderson transformation in the Start, $F(1,29)=0.36$, $p>0.5$, and in the Run, $F(1,29)=1.05$, $p>0.3$. In contrast, the PREE remained clear also following Anderson transformation. The presence of the PREE was supported in the Start by the significant main effect of Reinforcement, $F(1,29)=20.96$, $p<0.001$, and by the significant Reinforcement × Days interaction, $F(7,203)=4.69$, $p<0.001$; in the Run by the significant main effect of Reinforcement, $F(1,29)=16.33$, $p<0.001$, and by the significant interaction of Reinforcement × Days, $F(7,203)=2.83$, $p<0.01$; and in the Goal, by the significant main effect of Reinforcement, $F(1,29)=18.42$, $p<0.001$, and by the significant Reinforcement × Days interaction, $F(7,203)=2.42$, $p<0.001$.

DISCUSSION

The present experiments show that amphetamine does not affect the PREE in a multitrial procedure. This outcome was obtained using 6 daily trials with a 5-min ITI as well as 3 daily trials with a 20-min ITI. In addition, PREE remained intact when the drug was administered throughout acquisition and extinction or was confined to the acquisition stage. These results stand in marked contrast to those obtained with a 1 trial/day procedure, in which amphetamine was shown to disrupt the PREE (19,20) and may provide important clues regarding the effects of the drug on the processes underlying the development of PREE at short and long ITI's.

As was pointed out in the Introduction, the development of the PREE at short and long ITI's is assumed to be mediated by different processes, often termed Capaldian and Amselian, respectively (7, 9–11, 17). According to both theories, resistance to extinction of the PRF animals is determined by the reinforcement of responding in the presence of stimuli elicited by nonreinforcement (NR). However, the theories differ in the nature of these stimuli as well as in the learning processes assumed to take place during PRF training. According to Capaldi (4), PRF animals are reinforced for responding in the presence of memory traces of the preceding NR trials. According to Amsel (1,2), nonreinforcement elicited stimili (frustration) are conditioned to the apparatus cues, and PRF animals are reinforced for responding in the presence of the apparatus produced frustration stimuli. Thus, with short ITI's, a direct association is made on reinforced trials between NR-elicited stimuli and reinforcement, whereas with long ITI's, the association between NR-elicited stimuli and reinforcement is mediated via the apparatus cues. The fact that amphetamine disrupts PREE with long (24 hr) but not short (5 or 20 min) ITI's, suggests that the drug does not affect the direct association between NR-elicited stimuli and reinforcement, but disrupts the association between NR-elicited stimuli and the apparatus cues. In support of the latter, we showed that with a 24 hr ITI PRF animals failed to develop increased resistance to extinction when the administration of amphetamine was confined to the nonreinforced trials (20). In this context, it is of interest to mention the effects of amphetamine on latent inhibition (LI). In the LI paradigm, preexposure to a nonreinforced stimulus retards subsequent conditioning to that stimulus (16). Also in this paradigm, amphetamine disrupts the behavioral control by stimuli associated with nonreinforcement, i.e., the stimulus preexposed animals fail to show retarded conditioning to that stimulus. However, the abolition of LI is obtained only if the preexposure and conditioning stages are given 24 hr apart but not when the two stages are given in one session (21,22). It is reasonable to assume that the development of LI with 24-hr interval between preexposure and conditioning is dependent on contextual cues, i.e., an association between the nonreinforced stimulus and context, and it is apparently this association which is blocked by amphetamine.

The results with PREE and LI suggest that in learning tasks which involve mixed exposure to conflicting appetitive (reinforcement) and aversive (nonreinforcement) events, the time interval separating such exposures may be a critical variable for predicting the action of amphetamine. Additional support for this contention is provided by the finding that amphetamine does not disrupt the partial punishment effect (PPE) (18). The PPE consists of the fact that animals trained on partial punishment (PP) are subsequently more resistant to punishment than CRF controls (5). Thus, the PPE is analogous to the PREE but mild shocks are used instead of nonreinforcement. However, in the PP schedule, the ITI between punishment and reinforcement is very short (reinforcement is available within seconds following shock), and, under these conditions, amphetamine does not impair the development of resistance to punishment. In general, it is possible that short ITI's which allow a direct association between stimuli associated with aversive events (nonreinforcement or punishment) and reinforcement, ensure a stronger stimulus control by these stimuli. It is well documented that behavior under strong stimulus control is more resistant to the effects of amphetamine than behavior under weak stimulus control (12–15). In the case of the 1 trial/day vs. multitrial PREE, this may be a general feature, as also anxiolytics disrupt the former but leave the latter intact (6,10). In general, the differential effects exerted by amphetamine on the PREE at different ITI's, as well as on the PPE and LI, provide additional evidence that this drug exerts selective effects on behavior as a function of different task parameters, emphasizing its "cognitive" influences in addition to the "general stimulant" properties.

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