Pharmacology Biochemistry and Behavior, Vol. 41, pp. 309-315, 1992
Printed in the U.S.A.

0091-3057/92 $5.00 + .00

Amphetamine and the Multitrial Partial Reinforcement Extinction Effect (PREE) in an Operant Chamber: Procedural Modifications That Lead to an Attenuation of the PREE

JORAM FELDON[1] AND INA WEINER

Department of Psychology, Tel-Aviv University, Ramat-Aviv, Tel-Aviv, Israel 69978

Received 28 June 1990

FELDON, J. AND I. WEINER. *Amphetamine and the multitrial partial reinforcement extinction effect (PREE) in an operant chamber: Procedural modifications that lead to an attenuation of the PREE.* PHARMACOL BIOCHEM BEHAV **41**(2) 309-315, 1992. - The partial reinforcement extinction effect (PREE) consists of the fact that animals receiving partial reinforcement (PRF) exhibit higher resistance to extinction than animals receiving continuous reinforcement (CRF). In previous studies, we found that amphetamine (AMPH) did not affect resistance to extinction of PRF animals trained with a multitrial procedure, but abolished resistance to extinction of PRF animals trained with a 1 trial/day procedure. Based on theoretical distinctions regarding the processes underlying the development of increased resistance to extinction at short and long intertrial intervals, we suggested that AMPH disrupts the formation of a context-mediated association between stimuli associated with nonreinforcement and subsequent reinforcement. To examine further this possibility, we designed conditions in a multitrial PRF procedure that do not allow a direct association between stimuli associated with nonreinforcement and reinforcement, and thus promote a context-mediated association between them. Two experiments were conducted in an operant chamber. In experiment 1, instead of the conventional 50% schedule of reinforcement throughout PRF training, days of 33% schedule of reinforcement were interspersed with days of continuous reinforcement; in experiment 2, a block (5 days) of 50% PRF schedule was alternated with a block (5 days) of CRF training, given either prior to or following PRF. In experiment 1, interspersing days of CRF training with days of 33% reinforcement schedule led to an attenuation of the PREE in AMPH-treated animals. In experiment 2, control animals that received CRF training either prior to or following PRF training exhibited a PREE similar to animals trained on PRF alone. AMPH-treated animals trained on PRF alone showed a robust PREE, but failed to exhibit PREE in both the CRF-PRF and PRF-CRF conditions. These results show that whereas amphetamine-treated animals exhibit increased resistance to extinction when trained on a multitrial PRF schedule and transferred to extinction, the drug attenuates/abolishes the effects of PRF training on extinction when such a schedule is embedded in CRF training.

Partial reinforcement Continuous reinforcement Resistance to extinction Amphetamine

IN the partial reinforcement extinction effect (PREE) paradigm, animals are trained in the acquisition stage to perform an instrumental response, such as running in a straight alley or bar pressing, for food reward. One group, the continuous reinforcement (CRF), receives a reward on every trial. The second group, the partial reinforcement (PRF), receives a reward only on a certain proportion, typically random 50%, of the trials. In the second stage, the two groups are tested in extinction, that is, no rewards are delivered on any of the trials. The PREE refers to the fact that PRF animals show increased resistance to extinction as compared to CRF animals (13).

In a series of experiments, we tested the effects of 1 mg/kg D-amphetamine on the PREE using a 1 trial/day (26,30) or a multitrial (5,6) procedure. The results of these experiments revealed a different action of amphetamine on the PREE in the two procedures. In the 1 trial/day procedure, the PREE was abolished. This abolition was due to an absence of increased resistance to extinction in PRF animals, while the extinction in CRF animals was unaffected. Since the development of increased resistance to extinction in PRF animals is considered to reflect the fact that these animals learn to respond in the presence of stimuli associated with nonreinforcement (NR) (7,14), these findings indicated that amphetamine disrupts the effects of such stimuli on behavior. To substantiate further this conclusion, we tested the effects of amphet-

[1] Requests for reprints should be addressed to Dr. J. Feldon, Department of Psychology, Tel-Aviv University, Tel-Aviv, Israel 69978.

amine on the PREE using a multitrial procedure. In contrast to results obtained with the 1 trial/day procedure, amphetamine did not affect the multitrial PREE in both a runway (5) and an operant chamber (6). We suggested that this discrepancy reflects a different action of amphetamine on the processes underlying the development of PREE at short and long intertrial intervals (ITI's) (5,6).

At short ITI's, stimuli elicited by nonreinforcement (memory traces of NR) are associated directly with reinforcement (R) on reinforced trials (3,7,14). This process is evidently not affected by amphetamine, as the PREE at short ITI's remains intact under the drug. At long ITI's, the association between nonreinforcement-elicited stimuli and reinforcement is mediated via the context: NR-produced stimuli are conditioned to the apparatus cues, which are in turn associated with reinforcement on the reinforced trials (1,7,14). The fact that amphetamine abolishes the PREE at long ITI's indicates that this drug disrupts the formation of such context-mediated association.

To examine further this possibility, we designed conditions in a multitrial PRF procedure that were expected to promote a context-mediated association between NR-produced stimuli and reinforcement, with the expectation that under such conditions the multitrial PREE also would be abolished by amphetamine. Two experiments were conducted in an operant chamber. In experiment 1, instead of the conventional 50% schedule of reinforcement throughout PRF training, days of 33% schedule of reinforcement were interspersed with days of continuous reinforcement. In experiment 2, a block (5 days) of 50% PRF schedule was alternated with a block (5 days) of CRF training, given either prior to or following PRF. We assumed that the introduction of full days of CRF training would prevent a direct NR-R association since animals cannot remember the outcome of preceding trials, or their sequence, over days of training (14). Consequently, under these conditions, the formation of NR-R association would be mediated by contextual cues.

EXPERIMENT 1

METHOD

Subjects

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

Apparatus

Four Campden Instruments operant chambers with two retractable levers (the right-hand lever was out of the box throughout the experiment) were used. The 2.8-W houselight was lit throughout the experimental session. The boxes were equipped with pellet dispensers, which delivered one 45-mg Campden Instruments food pellet as reinforcement. The operation of the equipment and data collection were controlled by a micro-Vax minicomputer.

Procedure

All animals received several days of pretraining [modelled after (6)]. For the first 2 days, rats were given 15-min sessions during which the lever was retracted and food pellets were delivered on a variable-time (VT) 30-s schedule. From the third day of pretraining, the lever was introduced into the box and two reinforcement schedules were in effect concurrently: Food was delivered independently of animals' responding on a VT 30-s schedule and a CRF schedule was superimposed on the VT schedule. The free food schedule was discontinued after rats made 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. Following 10 reinforcements on FR-5, pretraining was completed. Following pretraining, acquisition stage was initiated. Acquisition lasted 12 days. On days 1, 2, 3, 6, 9, and 12, each daily session consisted of 10 discrete trials with an ITI of 60 s, and on days 4, 5, 7, 8, 10, and 11 the daily session consisted of 15 discrete trials with an ITI of 60 s. At the start of each session, the houselight was lit and the retractable lever was inserted into the box. Following five lever-presses, the tray light came on. As the rat inserted its head into the tray, the lever was retracted and, if scheduled, reward was delivered. The CRF animals received a reward on each of the daily trials. The PRF subjects received continuous reinforcement on days 1, 2, 3, 6, 9, and 12 and a quasirandom 33% schedule of reinforcement, i.e., 5 reinforced and 10 nonreinforced trials, on days 4, 5, 7, 8, 10, and 11.

Following acquisition, 4 days of extinction commenced. During extinction, all animals received 15 daily trials in a procedure identical to that of acquisition except that no rewards were delivered on any of the trials.

The data collected during the entire experiment consisted of three time measurements for each trial: 1) start time—the time between the insertion of the lever into the box and the first lever press; 2) run time—the time from the first press to the fifth; and 3) goal time—the time between the last press and tray entry. The procedure was programmed such that a maximal duration of 60 s was allowed for each of of the start, run, and goal times. If any of these times reached 60 s, the lever was retracted and the trial terminated. A score of 60 s 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 (ANOVA). Analyses were performed for the acquisition and extinction stages. Both analyses included three main factors: drug (amphetamine or placebo), reinforcement (CRF or PRF), and a repeated measurements factor of days (12 for acquisition and 5 for extinction). The analyses of the extinction data included the last day of acquisition.

Drug Injections

In pretraining, all animals received saline (0.3 ml) IP injections 15 min prior to each daily session. In acquisition and extinction, 1 mg/kg *d*-amphetamine sulfate (dissolved in saline at a concentration of 1 mg/ml) or saline was injected IP 15 min prior to each daily session.

Subjects were divided into 4 groups in a 2 × 2 design consisting of drug (amphetamine or placebo) and reinforcement (CRF or PRF). Two subjects (one placebo-PRF and one amphetamine-CRF) failed to lever press and were excluded from the experiment. Thus, the final group size were placebo-CRF (n = 9); placebo-PRF (n = 8); amphetamine-CRF (n = 8); amphetamine PRF (n = 9).

RESULTS

Acquisition

Fig. 1 presents daily mean log run times for the groups receiving the different reinforcement schedules (CRF or PRF)

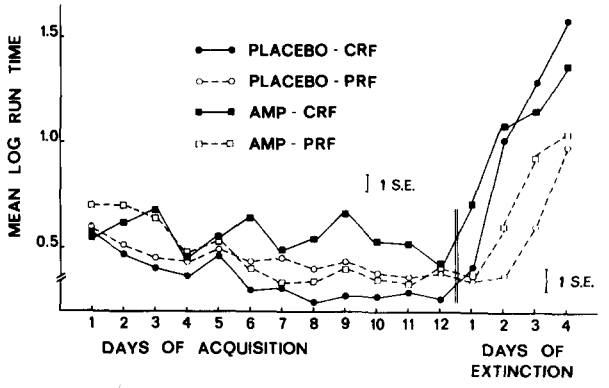

FIG. 1. Course of acquisition and extinction, expressed as mean log run time, for CRF and PRF animals in the placebo and AMP conditions. The bars on the left and right sides represent one standard error derived from the error term of the ANOVA of the acquisition and extinction data, respectively.

and drug injections (amphetamine or saline). These results are representative of the start and goal results. As can be seen, the amphetamine-CRF group exhibited slightly slower times to complete the five lever presses as compared to the placebo-CRF group, whereas the two PRF groups did not differ. This result was supported by the significant drug × reinforcement × days interaction in the run $F(11,330) = 2.86$, $p < 0.002$ and in the start $F(11,330) = 1.85$, $p < 0.05$. In the goal, although the same pattern emerged there were no significant main effects or interactions. At the end of acquisition, there were no significant differences among the four groups (see the one standard error bar on the left side of the figure).

Extinction

Figure 1 presents daily mean log run times for groups receiving the different reinforcement schedules (CRF or PRF) and drug injections (amphetamine or saline). These results are representative of the start and goal results. As can be seen, PREE, that is, faster run times of the PRF groups as compared to CRF groups, was obtained. This was supported in the run by the significant main effect of reinforcement $F(1,30) = 19.52$, $p < 0.001$ and by the significant reinforcement × days interaction $F(4,120) = 10.61$, $p < 0.001$. An identical picture emerged in the start and in the goal and was supported by the significant main effect of reinforcement $F(1,30) = 15.29$, $p < 0.001$ and $F(1,30) = 15.97$, $p < 0.001$ in the start and goal, respectively, as well as by the significant reinforcement × days interaction $F(4,120) = 6.74$, $p < 0.001$ and $F(4,120) = 6.86$, $p < 0.001$ in the start and goal, respectively. In addition, the analysis yielded a significant drug × reinforcement × days interaction in the run $F(4,120) = 4.05$, $p < 0.005$ and in the start $F(4,120) = 5.16$, $p < 0.001$. An inspection of Fig. 1 reveals that this interaction reflects an attenuation of the PREE in the amphetamine condition. This was due to the fact that the amphetamine-PRF group showed slower times to complete the five lever presses on days 2 and 3, as compared to placebo-PRF group, while on day 4 of extinction the amphetamine-CRF group showed faster times to complete the five lever presses as compared with the placebo-CRF group. Posthoc *t*-tests based on the error term derived from the ANOVA supported the presence of decreased resistance to extinction in the amphetamine-PRF group compared with the placebo-PRF group on day 2 ($p < 0.05$) and day 3 ($p < 0.005$), as well as increased resistance to extinction in the amphetamine-CRF group compared with the placebo-CRF group on day 4 ($p < 0.05$).

EXPERIMENT 2

METHOD

Subjects

The subjects were 56 male Wistar rats as in Experiment 1.

Apparatus

The same apparatus as in experiment 1 was used.

Procedure

All animals received several days of pretraining as in Experiment 1, followed by the acquisition stage. Acquisition lasted 10 days with each daily session consisting of 10 discrete trials with an ITI of 60 s. The CRF animals received a reward on each of the 10 trials. The PRF subjects received a reward on a quasirandom 50% schedule, that is, 5 reinforced and 5 nonreinforced trials. The 10 days of acquisition were divided into two sections of 5 days each. During each of these sections, either CRF or PRF training were given, creating four schedules of acquisition: 1) CRF throughout the 10 days of acquisition (CRF-CRF); 2) CRF training on days 1-5 and PRF training on days 6-10 (CRF-PRF); 3) PRF training on days 1-5 and CRF training on days 6-10 (PRF-CRF); 4) PRF training throughout the 10 days of acquisition (PRF-PRF). 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.

Data collection was identical to experiment 1. Analyses were performed for the acquisition and extinction stages. Both analyses included four main factors: drug (amphetamine or placebo), reinforcement 1 (CRF or PRF during the first 5 days of acquisition), reinforcement 2 (CRF or PRF during the last 5 days of acquisition), and a repeated measurements factor of days (10 for acquisition and 6 for extinction). The analysis of the extinction data included the last day of acquisition.

Drug injections

Drug injections were made as in Experiment 1.

Subjects were divided into eight groups in a 2 × 2 × 2 design consisting of drug (amphetamine or placebo), reinforcement 1 (CRF or PRF), and reinforcement 2 (CRF or PRF). Five subjects (one placebo CRF-CRF, one placebo PRF-PRF, one amphetamine CRF-CRF, one amphetamine PRF-CRF, and one amphetamine PRF-PRF) failed to lever press and were excluded from the experiment. Thus, the final group sizes were: placebo CRF-CRF ($n = 6$); placebo CRF-PRF ($n = 7$); placebo PRF-CRF ($n = 7$); placebo PRF-PRF ($n = 6$); amphetamine CRF-CRF ($n = 6$); amphetamine CRF-PRF ($n = 7$); amphetamine PRF-CRF ($n = 6$); amphetamine PRF-PRF ($n = 6$).

RESULTS

Acquisition

Figure 2 presents the daily mean log run times for the four placebo groups (top) and the four amphetamine groups (bottom). These results are representative of the start and goal

results. The 2 × 2 × 2 × 10 ANOVA's performed on the log start, run, and goal times yielded no significant main effects or interactions. As can be seen in Fig. 2, the course of acquisition was highly similar across the eight groups.

Extinction

Figure 2 presents daily mean log run times in the four placebo (top) and the four amphetamine (bottom) groups. These results are representative of start and goal results. Table 1 presents the significant outcomes of the 2 × 2 × 2 × 6 ANOVA's performed on the mean log start, run, and goal times. As can be seen, for each of the three time measures either a significant interaction of drug × reinforcement 1 × reinforcement 2 or of drug × reinforcement 1 × reinforcement 2 × days was obtained. An inspection of Fig. 2 indicates that these interactions reflect the following results: In the placebo animals, the three groups given PRF training, either in the first or in the second part of acquisition, exhibited increased resistance to extinction as compared to the group that received CRF training throughout acquisition. Posthoc one-tail *t*-tests revealed that all three PRF placebo groups (CRF-PRF, PRF-CRF, and PRF-PRF) showed significantly higher resistance to extinction in comparison with the CRF-CRF placebo group (all p's < 0.05). Thus, all placebo groups that received PRF training exhibited the PREE. In contrast, in amphetamine-treated animals, the only group that showed increased resistance to extinction was that trained on a PRF schedule throughout acquisition. The other two groups of animals, which received PRF training either prior to or following CRF training, extinguished in a virtually identical manner to animals that received CRF training throughout acquisition (except for the amphetamine PRF-CRF group, which showed a slight tendency toward increased resistance to extinction on day 3). Posthoc one-tail *t*-tests revealed that only the PRF-PRF amphetamine group showed a significantly higher resistance to extinction in comparison with the CRF-CRF amphetamine group ($p < 0.01$). Additional noteworthy features shown in Fig. 2 are: 1) the two CRF-CRF groups (placebo and amphetamine) and the two amphetamine groups that received PRF training before or after CRF exhibited a highly similar rate of extinction; 2) whereas the two amphetamine groups that received PRF training before or after CRF showed decreased resistance to extinction as compared with their placebo counterparts, the amphetamine group that received PRF training throughout acquisition showed increased resistance to extinction compared to its placebo controls. Thus, the three placebo groups that received PRF training in acquisition extinguished at a similar rate and demonstrated increased resistance to extinction compared with the amphetamine CRF-CRF group, the amphetamine PRF-CRF group, the amphetamine CRF-PRF group, and the placebo CRF-CRF group, whereas the amphetamine PRF-PRF group showed shortest times in extinction, that is, highest resistance to extinction. The same outcome is evident in Fig. 3, which depicts the mean log run times over the entire extinction period for the eight experimental groups.

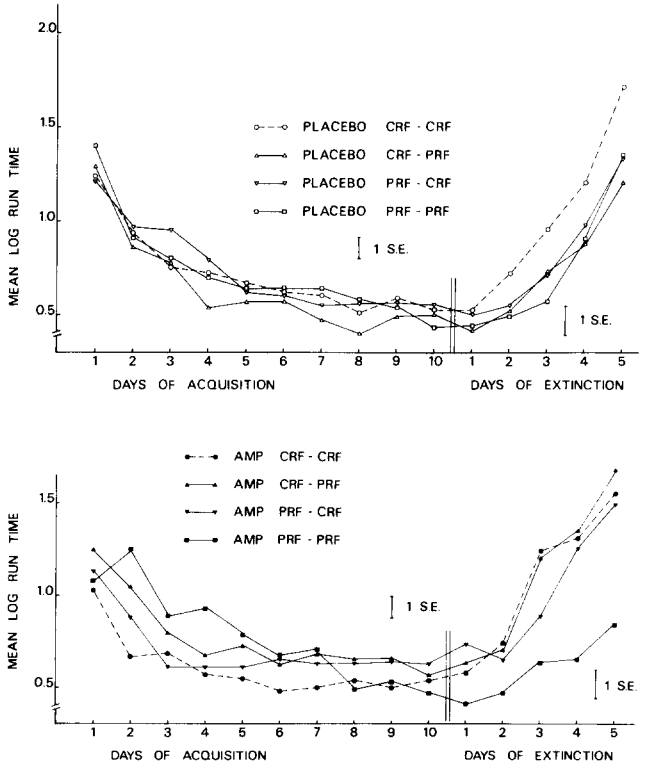

FIG. 2. Course of acquisition and extinction, expressed as mean log run time, for the four placebo groups (top) and the four amphetamine groups (bottom) in the four reinforcement conditions: CRF-CRF; CRF-PRF;PRF-CRF; and PRF-PRF. The bars on the left and right sides represent one standard error derived from the error term of the ANOVA of the acquisition and extinction data, respectively.

DISCUSSION

In our previous experiments using a multitrial PREE procedure, PRF animals were trained on a random 50% reinforcement schedule throughout acquisition. Under these conditions, amphetamine-treated (AMPH) animals exhibited a normal PREE (5,6). The results of experiment 1 indicated that interspersing days of CRF training with days of 33% reinforcement schedule led to an attenuation of the PREE in AMPH-treated animals, indicating that under conditions in which PRF training is embedded in extensive CRF training amphetamine impairs the development of increased resistance to extinction. Experiment 2 provided additional evidence for this suggestion. In this experiment, control animals that received CRF training either prior to or following PRF training exhibited a PREE identical to animals trained on PRF alone. AMPH-treated animals trained on a PRF schedule throughout acquisition exhibited the PREE. However, in marked contrast to saline animals, AMPH-treated animals failed to exhibit PREE in both the CRF-PRF and PRF-CRF conditions. This absence of the PREE is particularly conspicuous in view of the fact that PRF-PRF amphetamine animals exhibited a robust PREE even in comparison to saline PRF-PRF animals. It could be argued that the absence of the PREE in the CRF-PRF and PRF-CRF conditions was due to the fact that in these conditions animals received only 5 days of PRF training. However, we found that AMPH-treated animals trained on a 50% PRF schedule for 6 days showed a robust PREE (6).

Experiments that tested the effects of interpolating CRF training before or after PRF on resistance to extinction have yielded variable results (11,21,23), although the CRF-PRF sequence appears to lead to an attenuated PREE relative to the PRF-CRF sequence. It is difficult to compare the present results, obtained in an operant chamber, with previous studies

TABLE 1

SIGNIFICANT OUTCOMES OF THE 2 × 2 × 2 × 6 ANOVA'S WITH MAIN FACTORS OF DRUG, REINFORCEMENT 1 (CRF OR PRF ON DAYS 1-5 OF ACQUISITION), REINFORCEMENT 2 (CRF OR PRF ON DAYS 6-10 OF ACQUISITION), AND A REPEATED MEASUREMENTS FACTOR OF DAYS, PERFORMED ON THE LOGARITHMICALLY TRANSFORMED START, RUN, AND GOAL TIMES

	Start			Run			Goal		
Main Effect/Interaction	*F*	*df*	*p*	*F*	*df*	*p*	*F*	*df*	*p*
R1	5.02	1,43	=0.03	6.61	1,43	<0.02	6.04	1,43	<0.02
R2	3.71	1,43	=0.06	5.66	1,43	<0.03	3.03	1,43	<0.09
Dr × R1 × R2	3.86	1,43	<0.06	4.06	1,43	=0.05			
R1 × D	2.55	5,215	<0.03	2.84	5,215	<0.02	4.16	5,215	<0.002
R2 × D	2.58	5,215	<0.03						
Dr × R1 × R2 × D	3.56	5,215	<0.005	2.05	5,215	<0.08	2.29	5,215	<0.05

R1, reinforcement 1; R2, reinforcement 2; Dr, drug; D, days.

conducted in runways since acquisition variables have been shown to affect resistance to extinction differentially in runways and operant chambers (14). However, it is of interest to note that in the present experiment somewhat smaller resistance to extinction in the CRF-PRF condition as compared to the PRF-CRF condition was obtained in AMPH-treated but not in the saline animals. It should also be pointed out that the decreased resistance to extinction obtained in AMPH-treated animals trained with a CRF schedule is typically obtained in normal animals as a consequence of increasing the percentage of reinforcement or the number of reinforced trials in a PRF schedule (14,15,19). Clearly, the increase in the percentage of reinforcement in the present experiments was not sufficient to abolish the development of resistance to extinction in control PRF animals, but it did so in AMPH-treated PRF animals. Thus, AMPH animals appear more sensitive to increments in reinforcement level in a PRF schedule. Since amphetamine is known to enhance the rewarding properties of reinforcement or of stimuli associated with reinforcement [e.g., (10,22)] the present results could reflect such a reward-enhancing property of this drug. However, this possibility is unlikely in view of the results obtained in the PRF-PRF condition. If AMPH-treated animals are trained with a functionally higher value of reinforcement, PRF-PRF animals would be expected to show reduced resistance to extinction as compared to no-drug controls, yet they showed much higher resistance to extinction than controls. This result demonstrates, in accordance with our previous data and interpretation (5,6) that the processes underlying the development of increased resistance to extinction on a conventional multitrial PRF schedule are not disrupted and may even be facilitated by amphetamine.

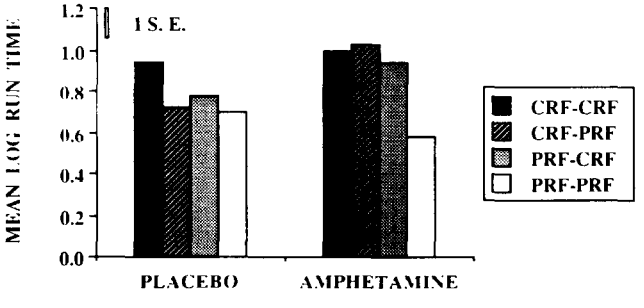

FIG. 3. Overall means of log run time throughout the extinction phase for the four placebo and four amphetamine groups in the four reinforcement conditions: CRF-CRF; CRF-PRF; PRF-CRF; and PRF-PRF. The bar on the top left corner represent one standard error derived from the error term of the ANOVA.

As noted in the introduction, increased resistance to extinction at short ITI's is believed to be primarily mediated by memory traces of nonreinforcement, as postulated by Capaldi (3,14). According to this view, during PRF training an association is formed between the outcome of preceding trials (memory traces of NR) and the outcome of subsequent trials (reinforced response, R). However, under conditions in which animals cannot remember the outcome of the preceding trial, or the sequence of preceding outcomes, for example, with long ITI's, the association between NR-elicited stimuli and the reinforced response becomes dependent on contextual cues (14), as elaborated by Amsel (1). Thus, NR-elicited stimuli become conditioned to apparatus cues that are then available for associating with the reinforced response whenever it occurs. Although in Amsel's theory the critical stimuli to which PRF animals learn to respond are conditioned frustration reactions elicited by NR, Mackintosh (14) points out that the stimuli in question may still be memory traces, which consist of a mixture of previous NR and R outcomes and whose retrieval depends on appropriate apparatus cues. It is quite clear that when full days of CRF training are given during PRF training animals cannot remember the outcomes of preceding NR trials or their sequence, and thus cannot associate directly these outcomes with the reinforced response. Rather, NR-elicited stimuli, be they memory traces or conditioned frustration reactions, are conditioned to the apparatus cues, which by virtue of their association with reinforcement come to control animals' responding on NR trials and subsequently in extinction. The fact that AMPH-treated animals that receive full days of CRF training combined with PRF training fail to exhibit increased resistance to extinction suggests that amphetamine disrupts the context-mediated association between NR-elicited stimuli and reinforcement. Consequently, whereas in normal animals NR-produced contextual stimuli cue the NR-reinforcement association and the accompanying instrumental response, under amphetamine this cuing property of the context is lost. We showed at the 1 trial/day procedure, which allows the administration of AMPH on either the reinforced or on the nonreinforced trials, that AMPH-treated

PRF animals failed to develop increased resistance to extinction when drug administration was confined to the nonreinforced trials (30). This demonstrates that the disruption of the NR-context-R connection is due to the failure to form an NR-context association.

In summary, the present results show that whereas amphetamine-treated animals show increased resistance to extinction when trained on a multitrial PRF schedule and transferred to extinction, this drug attenuates/abolishes the effects of PRF training on extinction when such a schedule is embedded in CRF training. This outcome, taken together with the differential effects of amphetamine on PREE at short vs. long ITI's, as well as on the PREE vs. the analogous partial punishment effect paradigm (25), provides further evidence that the behavioral effects of amphetamine can be markedly modulated by changes in experimental parameters, and emphasizes the cognitive effects of this drug as opposed to its nonspecific stimulating effects. Such cognitive effects are of particular interest in view of the fact that the behavioral actions of amphetamine administration in animals are considered to provide an animal model of schizophrenia (8,12,17,18). Although this model has relied primarily on the motor effects of amphetamine (hyperactivity and stereotypy), there has been also some success in inducing in animals cognitive alterations that resemble some features of the clinical syndrome, such as an inability to ignore irrelevant stimuli (20,31–33) and rapid switching of associations (24,27–29). The loss of the contextual control responsible for the development of increased resistance to extinction under amphetamine may provide an animal analogue of an additional central feature of schizophrenia, namely, a failure to use contextual cues or contextually generated expectations (2,4,9,16).

ACKNOWLEDGEMENTS

This study was supported by a grant from the Israeli Ministry of Health, Chief Scientist's Office, to J. Feldon and I. Weiner.

REFERENCES

1. Amsel, A. Frustrative nonreward in partial reinforcement and discrimination learning: Some recent history and a theoretical extension. Psychol. Rev. 69:306–328; 1962.
2. Anscombe, F. The disorder of consciousness in schizophrenia. Schiz. Bull. 13:241–260; 1987.
3. 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.
4. Chapman, L. J.; Chapman, J. P. Disordered thought in schizophrenia. New York: Prentice Hall; 1973.
5. Feldon, J.; Bercovitz, H.; Weiner, I. The effects of amphetamine on a multitrial partial reinforcement extinction effect (PREE) in a runway. Pharmacol. Biochem. Behav. 32:55–63; 1989.
6. Feldon, J.; Weiner, I. The effects of amphetamine on a multitrial partial reinforcement extinction effect (PREE) in an operant chamber. Pharmacol. Biochem. Behav. 32:65–69; 1989.
7. Gray, J. A. Elements of a two-process-theory of learning. London: Academic Press; 1975.
8. Gray, J. A.; Feldon, J.; Rawlins, J. N. P.; Hemsley, D. R.; Smith, A. D. The neuropsychology of schizophrenia. Behav. Brain Sci. 14:1–84; 1991.
9. Hemsley, D. R. An experimental psychological model for schizophrenia. In: Hafner, H.; Gattaz, W. F.; Janzavik, W., eds. Search for the causes of schizophrenia. Heidelbeg: Springer-Verlag; 1987:179–188.
10. Hill, R. T. Facilitation of conditioned reinforcement as a mechanism of psychomotor stimulation. In: Costa, E.; Garattini, S. eds. Amphetamine and related compounds. New York: Raven Press; 1970:781–795.
11. Jenkins, H. M. Resistance to extinction when partial reinforcement is followed by regular reinforcement. J. Exp. Psychol. 64: 441–450; 1962.
12. Kokkinidis, L.; Anisman, H. Amphetamine models of paranoid schizophrenia: An overview and elaboration of animal experimentation. Psychol. Bull. 88:551–579; 1980.
13. Lewis, D. J. Partial reinforcement: A selective review of the literature since 1950. Psychol. Bull. 57:1–28, 1960.
14. Mackintosh, N. J. The psychology of animal learning. London: Academic Press; 1974.
15. Morris, M. D.; Capaldi, E. J. Extinction responding following partial reinforcement: The effects of number of rewarded trials and magnitude of reward. Animal Learn. Behav. 7:509–513; 1979.
16. Patterson, T. Studies towards the subcortical pathogenesis of schizophrenia. Schiz. Bull. 13:555–576; 1987.
17. Robinson, T. E.; Becker, J. B. Enduring changes in brain and behavior produced by chronic amphetamine administration: A review and evaluation of animal models of amphetamine psychosis. Brain Res. Rev. 11:157–198; 1986.
18. Segal, D. S.; Schuckit, M. A. Animal models of stimulant-induced psychosis. In: Creese, I., ed. Stimulants: Neurochemical, behavioral and clinical perspectives. New York: Raven Press; 1983.
19. Seybert, J. A.; Baer, L. P.; Harvey, R. J.; Ludwig, K.; Gerard, I. C. Resistance to extinction as a function of percentage of reward: A reinforcement-level interpretation. Animal Learn. Behav. 7:233–238; 1979.
20. Solomon, P. R.; Crider, A.; Winkelman, J. W.; Turi, A.; Kamer, R. M.; Kaplan, L. J. Disrupted latent inhibition in the rat with chronic amphetamine or haloperidol-induced supersensitivity: Relationship to schizophrenic attention disorder. Biol. Psychiat. 16:519–537; 1981.
21. Sutherland, N. S.; Mackintosh, N. J.; Wolfe, J. B. Extinction as a function of the order of partial and consistent reinforcement. J. Exp. Psychol. 69:56–59; 1965.
22. Taylor, J. R. Robbins, T. W. 6-Hydroxydopamine lesions of the nucleus accumbens, but not of the caudate nucleus, attenuate enhanced responding with reward-related stimuli produced by intra-accumbens d-amphetamine. Psychopharmacology 90:390–397; 1986.
23. Theois, J.; McGinnis, R. W. Partial reinforcement before and after continuous reinforcement. J. Exp. Psychol. 73:479–481; 1967.
24. Weiner, I.; Ben-Horin, E.; Feldon, J. Amphetamine and the overtraining reversal effect. Pharmacol. Biochem. Behav. 24: 1539–1542; 1986.
25. Weiner, I.; Bercovitz, H.; Feldon, J. Amphetamine does not affect the partial punishment effect (PPE). Psychopharmacology 88:119–123; 1986.
26. Weiner, I.; Bercovitz, H.; Lubow, R. E.; Feldon, J. The abolition of the partial reinforcement extinction effect (PREE) by amphetamine. Psychopharmacology (Berl.) 86:318–323; 1985.
27. Weiner, I.; Feldon, J. Reversal and nonreversal shifts under amphetamine. Psychopharmacology 89:355–359; 1986.
28. Weiner, I.; Feldon, J.; Ben-Horin, E. Facilitation of discrimination transfers under amphetamine: The relative control by S^+ and S^- and general transfer effects. Psychopharmacology 93:261–267; 1987.
29. Weiner, I.; Feldon. J.; Ben-Shahar, O. Simultaneous brightness discrimination and reversal: The effects of amphetamine administration in the two stages. Pharmacol. Biochem. Behav. 25:939–942; 1986.

30. 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.
31. Weiner, I.; Lubow, R. E.; Feldon, J. Chronic amphetamine and latent inhibition. Behav. Brain Res. 2:285–286; 1981.
32. Weiner, I.; Lubow, R. E.; Feldon, J. Abolition of the expression but not the acquisition of latent inhibition by chronic amphetamine in rats. Psychopharmacology 83:194–199; 1984.
33. Weiner, I.; Lubow, R. E.; Feldon, J. Disruption of latent inhibition by acute administration of low doses of amphetamine. Pharmacol. Biochem. Behav. 30:871–878; 1988.