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Effects of post-training *d*-amphetamine on acquisition of an appetitive autoshaped lever press response in rats

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Abstract. This experiment examined the effect of post-training *d*-amphetamine on retention in an appetitive autoshaping conditioning situation. Harlan Sprague-Dawley rats were first given ten autoshaping trials, followed by either three or four additional sessions of 50 trials (70 s intertrial interval) on which the conditioned stimulus (the extension of an illuminated Plexiglas lever for 10 s) and unconditioned stimulus (a 45 mg food pellet), were paired. *d*-Amphetamine (1 or 2 mg/kg) or saline was administered IP either immediately or 2 h following training. Rats injected with 1 mg/kg *d*-amphetamine immediately after the first training session made significantly more responses during the conditioned stimulus presentation on the following daily session of 50 trials. Thus, the amphetamine-treated rats acquired the lever press response faster than those given only saline. The amphetamine effects were time dependent: no significant effects were found if the injection was delayed until 2 h following training. These results agree with the findings of other instrumental aversive facilitation studies and suggest that *d*-amphetamine may enhance retention of the classically conditioned components of autoshaping.

Key words: Autoshaping – Amphetamine – Appetitive conditioning – Facilitation of acquisition – Memory – Rats

Numerous studies have shown that retention can be enhanced by stimulant drugs administered immediately after training (McGaugh 1968, 1973). These effects are time dependent (McGaugh 1966). That is, treatments given following training are effective only if they are given in close temporal proximity to the training trial. Most studies to date have used some form of aversive conditioning, such as one-trial inhibitory avoidance conditioning. Further, few experiments have examined the effects of drugs on an explicit contingency (manipulated by the experimenter) between a conditioned stimulus (CS) and an unconditioned stimulus (US).

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Experiments using post-training administration of drugs are very rare in the Pavlovian literature. Benevento and Kandel (1967) and Cholewiak et al. (1968) reported that strychnine sulphate administered prior to conditioning trial enhanced the rate of acquisition of a nictitating membrane response in rabbits. Elisabetsky et al. (1979) found that post-trial injections of potassium chloride in the hippocampus of rats enhanced the "transfer" from Pavlovian to instrumental avoidance conditioning. Finally, Hernandez and Powell (1983) found that naloxone enhanced acquisition of a classically conditioned eyeblink response in rabbits.

The present study examined the effect of a CNS stimulant (*d*-amphetamine), given after training, on the acquisition of an autoshaped lever press response. Autoshaping (Brown and Jenkins 1968) procedures have been used to examine the interaction between Pavlovian and operant paradigms. A hungry animal (pigeon or rat) can learn to peck or press an illuminated manipulandum (key or lever) when its illumination is preceded by food presentation. Since the CS-US contingency is independent of the subject's behavior, the findings of autoshaping studies suggest that operant or instrumental acquired responses are controlled by Pavlovian or classical contingencies. For a review see Locurto et al. (1981).

Materials and methods

Subjects. The subjects were 35 male Harlan Sprague-Dawley (ARS) rats. Their ages ranged between 60 and 70 days upon their arrival in the laboratory. They were housed in individual cages and were maintained with water and food continuously available for 1 week. Over a period of 10 days their body weights were then reduced to 85%.

Apparatus. A standard sound-attenuated operant chamber for rats was used. The chamber was 25 cm wide, 29 cm long, and 25 cm high. A rat retractable lever (Coulbourn Instruments E21-03) was mounted 4 cm above the floor and 10 cm from the right or left wall, and required a minimum force of 10 g for operation. A receptacle (food-cup) for 45 mg Noyes rat pellets was 5 cm to the right of the lever and 3 cm above the floor. A magazine lamp was installed inside the top of the food-cup opening. A house light was located in the top left corner of the front wall, 29 cm from the floor. A masking noise was provided by a small speaker located in the right top corner. Solid-state

programming equipment was used for control and recording.

Auto-shaping training. The subjects were randomly assigned to one of five groups, each consisting of seven rats. In the first session (Day 1) of training, all animals received five free 45 mg food pellets. Once the subject ate the pellets, the first training trial began with the insertion (20 mm from the wall) of the illuminated Plexiglas lever for 10 s (conditioned stimulus, CS) followed immediately by one 45 mg food pellet (unconditioned stimulus, US); the intertrial interval (ITI) was 70 s. The first session (Day 1) consisted of ten trials and each session thereafter (either 4 or 5 days) consisted of 50 trials (CS-US presentations). All pairings of CS-US were independent of the animal's behavior. Following a response during the CS the lever was partially retracted from the conditioning chamber, a food pellet was delivered, and a new trial was initiated. Responses during the presence of the CS were recorded and transformed to a percentage of the total trials for each session. Also, latencies (s) for each response made during the CS presentation were recorded.

Drug treatment. Immediately after the first ten trials (Day 1), three groups received injections of either saline or *d*-amphetamine (1.0 or 2.0 mg/kg). Two additional groups received saline or *d*-amphetamine (1.0 mg/kg) 2 h following the training session. The amphetamine (Sigma Co.) was dissolved in sodium chloride (0.95) and injected in a volume of 1 ml/kg.

Results

Mean (%) performance of each group is presented in Fig. 1. Statistical analysis by 2-way ANOVA with repeated measures yielded significant differences for dose ($F=3.48$; $df=2,25$, $P<0.05$) days ($F=2.94$; $df=3,51$, $P<0.05$) and dose x days ($F=2.51$; $df=6,51$, $P<0.05$). No differences were found between any of the groups during the first session (Day 1) or second session (Day 2). However, a significant mean difference ($t=2.60$; $df=12$, $P<0.05$) was found between saline and the 1.0 mg/kg amphetamine group on Day 3 (left panel). A non-significant difference ($t=1.72$, $df=12$, $P<0.10$) between saline and the 1.0 mg/kg amphetamine groups was obtained on Day 4. The 2.0 mg/kg dose did not affect performance. The groups did not differ in response latencies on any day. There were no significant differences between the groups in behavioral measures when the amphetamine injection was delayed until 2 h post-training (right panel).

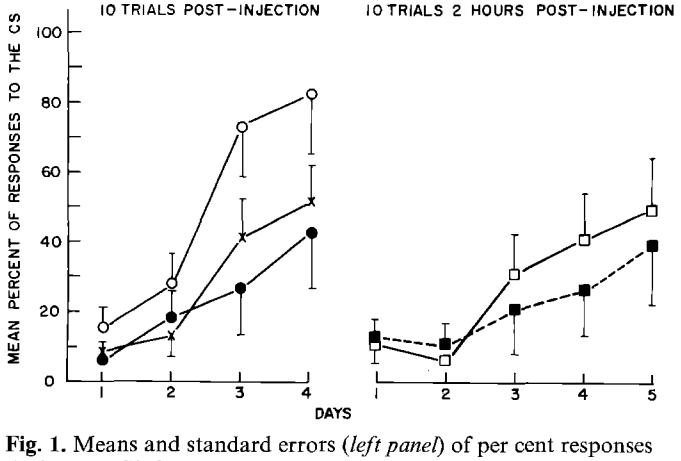

Fig. 1. Means and standard errors (*left panel*) of per cent responses during the CS for amphetamine given after ten trials. Means and standard errors (*right panel*) of per cent responses for amphetamine given 2 h after the first ten trials. Ten trials were given on Day 1 and 50 trials a day thereafter. *Left panel:* ● Saline; x 2 mg D-AMPH; o 1 mg D-AMPH. *Right panel:* ■ Saline; □ 1 mg D-AMPH

Discussion

The results of the present experiment agree with those of previous studies of the effects of post-training administration of amphetamine. Enhancement of retention is generally found with low doses, while higher doses are ineffective (Krivanek and McGaugh 1969; McGaugh 1973). The findings provide additional support for the view that amphetamine affects retention through influences on time-dependent memory storage processes (McGaugh 1966) and that the effects can be obtained in tasks using appetitive as well as aversive motivation.

Further, these results suggest that autoshaping may be a useful paradigm with which to evaluate CNS stimulant effects on memory. During the first 50 trials the CS elicited only a few responses. This finding agrees with that of Myer and Hull (1974), who reported less than 50% responding during the first 80 trials. Therefore, the amphetamine effect on lever pressing performance is not seen in the first 2 days, because of the low response rate. However, the animals clearly learn the CS-US contingency in these early trials (Williams and Williams 1969), and the response-US contingencies are maintained in the later trials. Thus, the emergence of a post-conditioning amphetamine effect on Day 3 appears to be due to an action of amphetamine on consolidation of information acquired on the 1st day when CS-US contingencies were presented independent of the animal's behavior.

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