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BRIEF COMMUNICATION

A Comparison of the Effects of Amphetamine on Fixed Interval Performance Maintained by Electrical Stimulation of the Brain Versus Food Reinforcement[1]

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CAREY, R. J. AND E. B. GOODALL. *A comparison of the effects of amphetamine on fixed interval performance maintained by electrical stimulation of the brain versus food reinforcement.* PHARMAC. BIOCHEM. BEHAV. 1(2) 237–239, 1973. –Rats with implanted unilateral hypothalamic bipolar electrodes were trained to bar press for both electrical stimulation of the brain (ESB) and food on a fixed interval (FI) 1-min schedule of reinforcement. A comparison in the same animals was made of the disruptive effects of *d*-amphetamine on FI performance maintained by these two reinforcers. Overall, FI remained more intact under the influence of amphetamine with ESB rather than with food reinforcement. The feasibility of using more complex schedules of reinforcement to study the effects of drugs on self-stimulation was demonstrated.

d-Amphetamine Fixed interval schedule Self-stimulation

IT HAS been repeatedly demonstrated that amphetamine markedly disrupts the temporal patterns of responding generated by fixed interval (FI) [2] or differential reinforcement of low rate (DRL) schedules of positive reinforcement [1,4]. A complication associated with this type of behavioral testing is that doses of amphetamine which affect temporal responding also have anorexic effects which affect the typical appetitive reinforcers utilized in these studies. In contrast to appetitive reinforcers, electrical stimulation of the brain (ESB) is an effective positive reinforcer which is enhanced by amphetamine [5]. It would be of interest, therefore, to determine the effect of amphetamine on fixed interval responding reinforced by ESB. In this study food-deprived animals were trained on a fixed interval schedule with either ESB or food as the reinforcer. The effects of several doses of amphetamine were compared with the same animals on fixed interval responding generated by the two types of positive reinforcement.

METHOD

Animals

Four male, Long-Evans rats, weighing 345 and 380 g at the start of the experiment, were used. Throughout the experiment rats were housed separately in a temperature- (70° ± 4°), humidity- (60% ± 10%), and illumination- (12-hr light, 12-hr dark) controlled room. Following recovery from surgery the animals were maintained at 85% of

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their preoperative body weight by restricting food intake. Water was always available in the home cage. Only two animals completed all phases of testing so this report is limited to the results obtained with these two animals.

Surgery

All rats were implanted with bipolar stainless steel electrodes insulated except for the cross-sectional area at the tip. In each rat one electrode was implanted unilaterally in the lateral hypothalamic area. Surgery was performed under ether anesthesia with the aid of a Kopf stereotaxic instrument. The stereotaxic coordinates used were: 3.0 mm posterior to bregma, 1.3 mm lateral to the midline, and 8.3 mm below the skull with the incisor bar positioned such that the skull was level between bregma and lambda. An intramuscular injection of 200,000 units of procaine penicillin was given following surgery.

On completion of experimentation brain lesions were made through the implanted electrodes while animals were under ether anesthesia. Anodal current of 2 mA for 10 sec was used to generate the lesions. The rats were then perfused intracardially with 0.9% saline followed by 10% Formalin. After fixation in 10% Formalin, brains were sectioned and electrode tip placement was verified in the lateral hypothalamus.

Apparatus

All testing was done in two 10 1/2 x 12 x 9 1/2 in. operant chambers housed individually in sound-attenuating enclosures (LVE No. 1417). One chamber was used for ESB reinforcement and was equipped with two 1 1/8 x 3/8 in. levers mounted 5 1/2 in. apart on one panel. Levers projected 1 1/4 in. into the chamber and required a force of 15 g to activate an attached microswitch. A mercury-swivel commutator mounted above the chamber connected the electrode to the stimulation equipment. The second chamber contained a single lever and food cup mounted on one panel. A pellet feeder which dispensed 45 mg P. J. Noyes lab rat pellets provided reinforcement in this chamber. Each chamber was illuminated by a 15 W lamp mounted at the top center of the side panel.

A Grass Brief Pulse Stimulator Model BPS 1 set to deliver a bipolar square wave of 60 Hz and 0.2 msec duration served as the source of current for brain stimulation. Applied voltage and current, calculated from the voltage drop across a 1 kΩ resistor in series with the animal, were monitored continuously on an oscilloscope. A stimulus train of 0.5 sec duration reinforced appropriate lever responses. Relays and switching circuits with timers and counters tabulated responses and controlled session duration.

PROCEDURE

One week after surgery training to lever press for brain stimulation was begun. During this period only one lever was present in the chamber and each response was reinforced. Once stable performance at an optimal rate of responding was achieved across daily 30 min test sessions, a second lever was introduced into the chamber. Using a procedure adapted from Pliskoff, Wright, and Hawkins [3], stimulation was now made available on a chained FI-continuous reinforcement 10 (CRF 10) schedule. During the FI segment of the schedule, the house light was off and the reinforcement (left) lever was inactive. Responses on the right lever were without effect during this interval, but the first response following termination of the interval turned on the house light and activated the reinforcement lever. Each of 10 responses on the left lever was reinforced during the period of chamber illumination, and the FI segment of the schedule was reinstated immediately after the 10th reinforcement. The FI duration, set initially at 15 sec, was increased to 1 min in 15-sec increments by giving two 30-min sessions at each duration. Training on this schedule, FI 1-CRF 10, continued until performance was stable across daily 30-min sessions.

Concurrently a feeding regimen was established to maintain animals at 85% of their preoperative body weight. Animals were trained to lever press for food pellets using a procedure identical to that used for brain stimulation reinforcement except that a single lever was used throughout food reinforced testing. During the FI segment of the schedule the house light was off and lever responses were without effect. The first response following termination of the FI turned on the house light and the next response produced delivery of a food pellet and reinstated the FI segment of the schedule. Thus, responding for food was reinforced on a FI 1-CRF 1 schedule until stable performance during daily 30-min sessions was obtained.

After this initial training, animals received daily two 30-min test sessions separated by a 30-min time-out period spent in the home cage. Sessions began with reinforcement available immediately to the animal, and on a given day the same reinforcer was used for both test sessions. Responses made during successive 15-sec class intervals of the FI 1 and the total number of reinforcements obtained were counted. Testing continued on this schedule alternating type of reinforcer daily. Once stable performance during each daily session for each reinforcer was obtained, drug test sessions were interspersed with nondrug daily sessions. On a drug test day a subcutaneous injection of *d*-amphetamine HCL (K and K Laboratories, Jamaica, N.Y.) in 0.9% saline solution was given immediately after the first 30-min test session and its effect was observed during the session following 30 min later. Drug doses of 1, 2, and 3 mg/kg body weight were administered in ascending order with at least 3 days between injections. Testing was alternated such that observation of drug effects on responding for both types of reinforcement was made before increasing drug dose level, and continued until each animal had been tested with each of the doses under both reinforcement conditions.

RESULTS

The FI response distribution in successive 15-sec class intervals for both animals that completed testing is summarized in Fig. 1. Baseline data represent the mean ± 1 standard deviation (SD) of all nondrug 30-min test sessions, and numbers beside each curve indicate amphetamine dose. The data show the typical scalloped response pattern under nondrug conditions for both ESB and food pellet reinforcement with no consistent differences in overall rate between the two reinforcers. All amphetamine dose levels markedly increased responding in each class interval for ESB. Although the nondrug scalloped function was dramatically changed at each dose level, responding did increase as the class interval increased. In contrast, for food reinforcement the interval response gradient was flatter across dose levels.

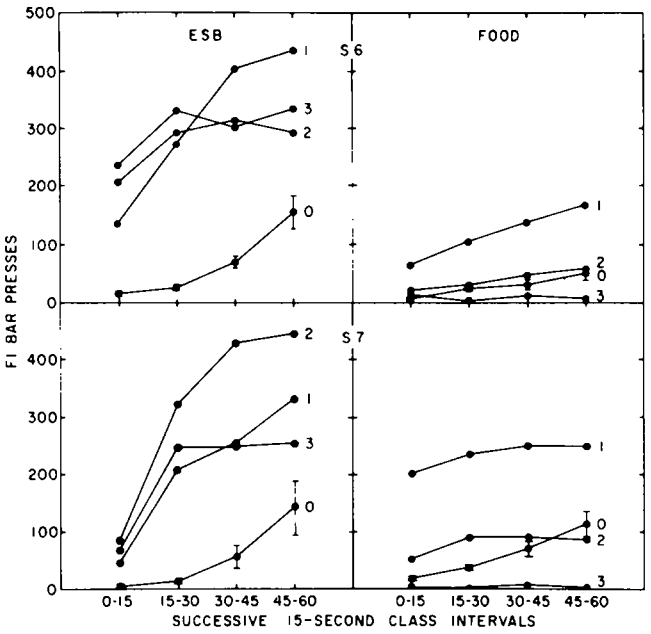

FIG. 1. Individual FI bar-pressing results in successive 15-sec intervals with 1.0, 2.0, and 3.0 mg/kg doses of *d*-amphetamine as well as means and standard deviations for the zero or nondrug sessions are indicated.

The dose-response curve (Fig. 2) indicated a marked difference in drug effect on total responding for ESB and food pellets. While all doses produced a 3–5 fold increase in responding for ESB, responding for food was increased only by the 1 mg/kg dose. The 2 mg/kg dose produced no change in rate of responding for food, and the 3 mg/kg dose nearly completely eliminated responding. The mean number of nondrug session ESB and food pellet reinforcements obtained were respectively: 240, 28 for S6, and 239, 28 for S7. The ESB and food reinforcements for the 1, 2 and 3 mg/kg drug test sessions were respectively: 260, 250, 260, and 28, 27, 12 for S6, and 270, 270, 260, and 29, 27, 6 for S7. Thus, large differences in response rates were not accompanied by changes in number of reinforcements obtained except during the decreased food-pellet responding at high drug doses.

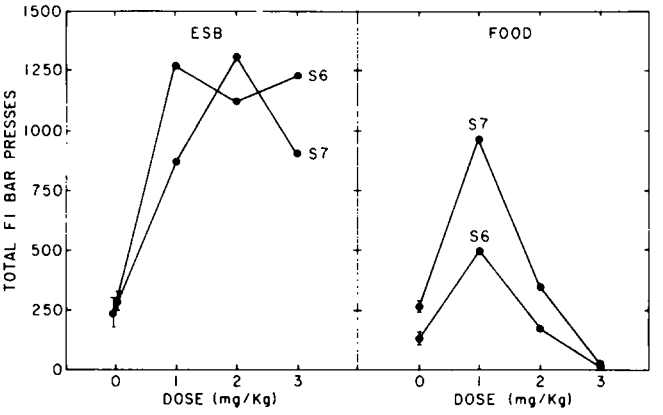

FIG. 2. Individual FI bar-pressing results for total session responding under amphetamine are shown along with means and standard deviations of responding in the nondrug sessions.

Electrode implants remained intact, and self-stimulation at currents of 180 and 200 μa for animals S6 and S7, respectively, was maintained unchanged throughout testing.

DISCUSSION

The ESB proved to be a highly effective reinforcer in generating the scalloped temporal response pattern characteristic of an FI schedule. As with appetitively reinforced FI schedules amphetamine markedly disrupted the temporal response pattern when ESB was used as the reinforcer. The temporal response pattern developed under ESB, however, was relatively less disrupted than the response pattern maintained by food deprivation. Furthermore, for amphetamine this study also shows that behavior can be maintained under substantially higher doses with ESB than with appetitive reinforcers, a finding which offers additional opportunities for investigation of this drug. The use of ESB as a reinforcer in drug studies has generally been limited to CRF schedules. As this study shows, however, more complex schedules can be utilized. Thus, it would seem desirable to have the effects of drugs on ESB examined with more sophisticated schedules than simple CRF schedules.

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