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Neither non-contingent electric footshock nor administered corticosterone facilitate the acquisition of methamphetamine self-administration

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Abstract

Previous research has indicated a role for the hypothalamo–pituitary–adrenal (HPA) axis in the acquisition of intravenous cocaine self-administration since both exposure to stressors and exogenous injections of corticosterone facilitate this behavior. The present experiment was designed to determine whether electric footshock or pretreatment with corticosterone would produce similar effects on the acquisition of methamphetamine self-administration in male Wistar rats. Following initial food training, the rats were allowed to self-administer methamphetamine in ascending doses (0.0075–0.12 mg/kg/infusion) that were doubled weekly. Neither non-contingent electric footshock nor treatment with corticosterone (2.0 mg/kg, i.p.) affected the lowest dose at which the rats first acquired methamphetamine self-administration (0.015 mg/kg/infusion). The treatment groups all had similar inverted "U"-shaped acquisition curves typical of psychostimulants. Although these experiments do not indicate a major role for the HPA axis in the acquisition of methamphetamine self-administration, more studies need to be conducted to further evaluate the effects of the HPA axis on the acquisition of methamphetamine self-administration before a potential role can be ruled out.

Keywords: HPA axis; Corticosterone; Electric footshock; Methamphetamine; Acquisition; Self-administration; Reward

1. Introduction

Studies using animal models of self-administration have found that the acquisition of psychostimulant self-administration is increased in rats exposed to stress. Repeated tail pinch (Piazza et al., 1990), social stress (Tidey and Miczek, 1997; Miczek and Mutschler, 1996; Haney et al., 1995), and social isolation (Howes et al., 2000; Kosten et al., 2000; Schenk et al., 1987) have all been found to accelerate the acquisition of psychostimulant self-administration. However, while pre-clinical research has investigated the effects of stress on the acquisition of cocaine and amphetamine self-administration, there have been no published reports on the effects of stress on methamphetamine self-administration.

Previous research conducted by our laboratory has shown that non-contingent electric footshock facilitates the acquisition of cocaine self-administration (Goeders and Guerin, 1994). The acquisition dose–response curve for rats receiving non-contingent footshock was shifted upward and to the left compared to rats receiving contingent footshock or non-shocked controls, indicating that these rats were more sensitive to low doses of cocaine. Plasma corticosterone was positively correlated with cocaine self-administration in all three groups at the 0.125 mg/kg/infusion dose of cocaine, the dose at which some rats acquired self-administration. Rats exposed to non-contingent footshock exhibited the highest plasma corticosterone and readily acquired self-administration at the 0.125 mg/kg/infusion dose. Later experiments were designed to explore the effects of adrenocorticosteroids on the acquis-

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ition of cocaine self-administration (Mantsch et al., 1998). In these experiments rats receiving daily injections of vehicle or corticosterone (2 mg/kg, i.p.) were presented with ascending concentrations of cocaine (0.031–0.5 mg/kg/infusion). Corticosterone pretreatment facilitated the acquisition of cocaine self-administration, indicating that elevated plasma corticosterone influences the acquisition of cocaine self-administration.

The present experiments were therefore designed to assess the effects of stress and the subsequent activation of the HPA axis on the acquisition of methamphetamine self-administration. Stress, in the form of non-contingent electric footshock was used to activate the HPA axis and thereby elevates plasma corticosterone. The effects of parentally administered corticosterone on the acquisition of methamphetamine self-administration were also evaluated.

2. Materials and methods

2.1. Subjects

Sixty, male Wistar rats, (Harlan Sprague–Dawley) 80 to 100 days old at the start of the experiment were used. All rats were housed in individual cages equipped with a laminar flow unit and air filter in a temperature- and humidity-controlled AAALAC-accredited animal care facility on a reversed 12-h light–dark cycle (lights on at 7:00 PM). Rats were maintained at 85% to 90% of their free-feeding body weights by presentations of food pellets (P.J. Noyes; 45 mg) during behavioral sessions when applicable and/or by supplemental feeding (Purina Rat Chow) and had access to water ad libitum. All procedures were approved by the LSUHSC-S animal care and use committee and were carried out in accordance with the NIH "Principles of Laboratory Animal Care" (NIH publication No. 85-23).

2.2. Venous catheterization and drug delivery

Each rat was implanted with a chronic indwelling jugular catheter under sodium pentobarbital anesthesia (50 mg/kg, i.p.) with methylatropine nitrate pretreatment (10 mg/kg, i.p.) using previously reported procedures (Koob and Goeders, 1989; Goeders et al., 1998). The animals were also injected with sterile penicillin G procaine suspension (75,000 U, i.m.) immediately before surgery, and they were allowed a minimum of 4 days to recover following surgery. The catheter (0.3048 mm i.d.×0.635 mm o.d., silicone tubing) was inserted into the right posterior facial vein and pushed down into the jugular vein until it terminated outside the right atrium. The catheter was anchored to tissue in the area and continued subcutaneously to the back where it exited at the base of the skull. The catheter was connected to a 22-gauge guide cannula (Plastic Products) which was mounted to the top of the skull using dental acrylic and stainless-steel screws for attachment of a leash. The stainless-steel spring leash (Plastic Products) was attached to the guide cannula assembly and to a leak-proof fluid swivel suspended above the operant chamber. Tubing connected the swivel to a 20-ml syringe in a motor-driven pump (Razel) located outside the sound attenuating enclosure. The swivel and leash assembly was counter-balanced to permit relatively unrestrained movement of the animal and was connected during all experimental sessions. At the end of each session, the leash was disconnected, the catheter was filled with streptokinase (816,000 IU) to inhibit the formation of blood clots and a dummy cannula was inserted into the guide before the rat was returned to its home cage. The patency of the catheters was tested immediately after the end of the session each Wednesday. If blood could be obtained via the catheter, then it was judged to be patent. If not, then the rat was injected via the catheter with methohexital sodium (1.5 mg, i.v.). An immediate light anesthesia indicated that the catheter was functional.

2.3. Apparatus

Standard plastic and stainless-steel operant conditioning chambers contained within sound-attenuating enclosures (Med-Associates) were used to run the behavioral experiments. Each experimental chamber was equipped with two retractable response levers (Med-Associates) mounted on either side of the chamber, with a stimulus light located above each lever. The enclosures contained an exhaust fan that supplied ventilation and white noise to mast extraneous sounds. An IBM-compatible computer and interface system (Med-Associates) was used to program the procedures and collect the experimental data.

2.4. Food and self-administration training

The rats were initially trained to respond for food pellets (45 mg) during daily 1-h test sessions for the first week. During these sessions, the food response lever was extended into the chamber and the corresponding lever light illuminated to indicate availability of food reinforcement. Each response on the food lever resulted in a brief darkening of the food stimulus light (0.6 s) and the delivery of a single food pellet. Sessions were terminated after 60 min or when 100 food pellets were delivered. The first day of the week (Monday) remained a food training session throughout the experiment to maintain lever-pressing behavior and as a control for the potential nonspecific effects of the various treatments.

During daily 1-h methamphetamine acquisition sessions, the drug response lever was extended into the chamber with the corresponding stimulus light above the lever illuminated. Responding on the drug lever (fixed-ratio 1) resulted in an infusion of saline or methamphetamine (200 μl over