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Research report

Sucrose intake enhances behavioral sensitization produced by cocaine

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Abstract

Many studies have reported relationships between the intake or preference for sweets and the effects or self-administration of drugs of abuse. This study was conducted to determine whether intermittent access to sucrose would alter the activity response to an injection of cocaine (15 mg/kg, i.p.) or the degree to which repeated cocaine injections produce behavioral sensitization. Nondeprived rats were given 1 h access to granulated sucrose, ground chow, or alternating sucrose and chow for 38 days. Activity levels were measured after injections of saline and cocaine. Rats were also tested after a total of seven cocaine injections, and again 14 days later with no intervening treatments. There was an on overall facilitation of the response to cocaine in rats exposed to sucrose, compared to rats exposed only to ground chow. Subsequent analyses indicated that after the seventh cocaine injection, there was a significant increase in activity of the sucrose group early in the session (compared to the chow group). When tested 14 days later, there was a prolongation of the effect of cocaine in the sucrose group. These results are in partial agreement with the results of others on amphetamine-elicited activity and suggest that some degree of potentiation or cross-sensitization between sucrose and psychostimulants is possible.
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Topic: Drugs of Abuse: Cocaine

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1. Introduction

The preference or intake of sucrose or saccharin has been reported to be predictive of subsequent levels of drug self-administration in animals, and altered preferences for sweets have been observed in human subjects during drug dependence or soon after the beginning of drug abstinence [7,15,16,26,28,39]. Access to sweet solutions reduces drug self-administration [5,6], and long-term intake of sucrose enhanced opioid- or amphetamine-induced conditioned place preferences as well as opioid-induced antinociception [29,53]. A daily feeding schedule in which a period of food deprivation alternated with a period of access to food and a glucose solution produced a change in dopamine and opioid receptor binding and, following injections of naloxone, produced an opioid-like withdrawal syndrome [10,11]. A potential explanation for the relationships among sweet food/fluid intake and drug reward and drug dependence is that palatable foods and many drugs of abuse activate the same or overlapping neural circuits. This explanation is supported by studies that have shown that the intake of palatable substances causes an increase in extracellular dopamine in the nucleus accumbens, an effect observed with most drugs of abuse [12,19,55,56].

One feature common to many drugs of abuse is behavioral sensitization, wherein the behavioral effects of a drug increase after repeated administration. In animals, sensitization can be observed with measures of activity, drug self-administration and conditioned place preference [22,27,34,52]. Sensitization is accompanied by, and is likely mediated in part by changes in dopaminergic and glutaminergic systems at both the synaptic and intracellular level [4,50,54]. Cross-sensitization can occur between drugs of different pharmacological classes. For example, injections

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of amphetamine into the ventral tegmental area produced a sensitized locomotor response to systemic morphine [51]. The acquisition of cocaine self-administration was facilitated by prior injections of caffeine, amphetamine or nicotine [23,24], and repeated injections of morphine enhanced the conditioned place preference caused by amphetamine or cocaine [34]. Behavioral sensitization can also be produced by non-pharmacological means. Prior uncontrollable shock caused an increase in amphetamine-induced rotation and potentiated amphetamine-induced stereotypy [37,43]. The acquisition of cocaine and amphetamine self-administration was increased by tail-pinch, footshock and social stress, which suggests that stress sensitizes the reinforcing effects of these drugs [14,42,46]. Lett [33] found that ingestion of a sucrose/saccharin mixture prior to and during the course of conditioned place preference (CPP) training enhanced the place preference produced by morphine, and, as mentioned above, sucrose enhanced opioid- or amphetamine-induced conditioned place preferences [53].

Recently, Avena and Hoebel [2] reported that a daily feeding regimen consisting of 12 h of food deprivation followed by 12 h access to chow and 10% sucrose solution potentiated the locomotor activating effects of amphetamine. This is somewhat reciprocal to their earlier finding that rats given repeated injections of amphetamine showed increased intake of sucrose [1]. The present study was performed to determine whether repetitive intake of sucrose can influence cocaine-induced behavioral activation and/or behavioral sensitization to cocaine. Aside from the different psychostimulant used, notable differences from the Avena and Hoebel [2] study include the use of granular sucrose in the absence of food deprivation and a determination of the effects of sucrose access on repeated injections of cocaine.

2. Materials and methods

2.1. Animals

Male Sprague–Dawley rats (Zivic Laboratories, Zelienople, PA) were individually housed in stainless steel cages and given standard lab chow and water ad libitum except where noted. Animals were allowed to adapt to the lab conditions for at least one week before the study began. This study was approved by the Neuropsychiatric Research Institute Animal Care and Use Committee and conducted in accordance with the *Guide for the Care and Use of Laboratory Animals* (National Research Council, revised 1996).

2.2. Sucrose/Chow pre-exposure

Approximately 4 h into the light cycle (lights on at 0700 h), food hoppers were removed from the cages and a glass jar containing either granulated sucrose or ground lab chow was attached to the floor of each cage. After 1 h, these jars were removed, and the hoppers containing pelleted chow were replaced. This procedure was repeated daily for 38 days. For one group of rats (SUCR group), the jar contained sucrose during every presentation. A second group received a jar containing powdered chow during every presentation (CHOW group), and a third group received sucrose and powdered chow on alternating days (ALT group). Intake (corrected for spillage) was measured for 2 consecutive days every 6 days throughout the 38-day exposure period. After this exposure period, all rats were maintained on ad libitum chow and water for the remainder of the study. The study was performed in two cohorts of 24 rats each, with each cohort containing equal numbers of rats in the three experimental groups. All results are based on pooled data (nb = 16/gp). On the first day of diet exposure, mean body weights were 353 ± 8, 359 ± 9 and 356 ± 8 g for the CHOW, ALT and SUCR groups, respectively.

2.3. Measurement of activity

Activity was measured in eight 17 × 17-in. chambers with clear plastic walls and a solid, smooth floor (Med Associates, St. Albans, VT). The chambers were individually housed in sound-attenuating cubicles equipped with a house light and a ventilation fan. Two banks of 16 infrared photobeams and detectors, mounted at right angles 3.5 cm above the floor, detected horizontal activity. An additional 16-beam array mounted 12.5 cm above the floor detected vertical activity. Activity Monitor software (Med Associates) was used to count photobeam breaks at 10-min intervals. This software subdivides total counts into stereotypic and ambulatory counts according to the repetitive (stereotypic) vs. sequential (ambulatory) patterning of the beam-breaks. Specifically, a box-shaped zone (4 × 4 in) is constructed around the computed center of the rat. Beam-breaks within this box are considered as stereotypic. Once three beam-breaks are recorded outside of the zone that occur in less than 500 ms, the rat is considered ambulatory, and these and other beam-breaks are classified as ambulatory counts until the rat stops for at least 500 ms (at which time the box-shaped zone is re-centered on the rat).

2.4. Experimental protocol

On the day following the final sucrose/chow pre-exposure, rats were placed in the activity chambers for 60 min, after which they were given an intraperitoneal (i.p.) injection of 0.9% saline and returned to the chambers for an additional 60 min. An identical procedure was followed on the next day, with the exception that cocaine hydrochloride (15 mg/kg) was injected rather than saline. On each of the 5 days after this cocaine trial, rats were given injections of cocaine (15 mg/kg) and returned to their home cages without measuring activity. One and fifteen days after the final home cage injection of cocaine, rats were again tested

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