Drug and Alcohol Dependence 177 (2017) 48–53

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

The effects of social contact on cocaine intake in female rats

Andrea M. Robinson, Gaylen E. Fronk, Huailin Zhang, Scott Tonidandel, Mark A. Smith*

Department of Psychology and Program in Neuroscience, Davidson College, Davidson, NC, USA

ARTICLE INFO

Keywords:
Behavioral economics
Demand curve
Estrous
Substance use
Social environment
Social learning

ABSTRACT

Background: Studies conducted in male rats report that social contact can either facilitate or inhibit drug intake depending on the behavior of social partners. The purpose of the present study was to: (1) examine the effects of social contact on cocaine intake in female rats, (2) examine the behavioral mechanisms by which social contact influences cocaine intake, and (3) examine whether the estrous cycle moderates the effects of social contact on cocaine intake.

Methods: Female rats were assigned to either isolated or pair-housed conditions in which a social partner either had access to cocaine (cocaine partner) or did not have access to cocaine (abstinent partner). Pair-housed rats were tested in custom-built operant conditioning chambers that allowed both rats to be tested simultaneously in the same chamber.

Results: Rats housed with a cocaine partner self-administered more cocaine than isolated rats and rats housed with an abstinent partner. A behavioral economic analysis indicated that these differences were driven by a greater intensity of cocaine demand (i.e., greater intake at lower unit prices) in rats housed with a cocaine partner. Multivariate modeling revealed that the estrous cycle did not moderate the effects of social contact on cocaine intake.

Conclusions: These findings indicate that: (1) social contact influences cocaine self-administration in females in a manner similar to that reported in males, (2) these effects are due to differences in the effects of social contact on the intensity of cocaine demand, and (3) these effects are consistent across all phases of the estrous cycle.

1. Introduction

Peers have a strong influence on an individual's likelihood of using drugs (Bahr et al., 2005; Simons-Morton and Chen, 2006). According to social learning theory, an individual learns to take drugs in small, informal groups (Bahr et al., 1998; Petraitis et al., 1995). In these settings, individuals are taught through imitation and reinforcement to hold attitudes that are favorable or unfavorable to drug use (Reed and Rountree, 1997). Indeed, individuals may experiment with drugs or alcohol to gain peer approval, but they may also stop using drugs or adopt anti-drug norms because of peer pressure (Teunissen et al., 2012). Adolescent males and females are particularly vulnerable to social influence, but it is thought that adolescent girls are more likely to succumb to peer influence because they tend to have more interpersonal relationships than boys (Downs, 1985).

Preclinical studies have shown that the social environment is a contributing factor to drug use (see reviews by Bardo et al., 2013; Neisewander et al., 2012; Strickland and Smith, 2015; Zernig et al., 2013). For instance, our laboratory has used modified operant conditioning chambers to examine intravenous drug self-administration in multiple rats at the same time and in the same chamber. Using these chambers, we found that cocaine self-administration was facilitated in male rats paired with a cocaine-using partner and inhibited in male rats paired with an abstaining partner (Smith, 2012). In addition, an experienced cocaine-using partner facilitated the acquisition of cocaine self-administration whereas an abstaining partner inhibited the acquisition of cocaine self-administration and reduced the escalation of cocaine intake over time (Robinson et al., 2016; Smith et al., 2014). Taken together, these data emphasize the critical role of the social environment in drug self-administration in males. These findings have not yet been extended to females, which is relevant given the increasing prevalence of substance use disorders in females (Brady et al., 2009; Greenfield et al., 2010) and the fact that females might be more vulnerable to social factors that influence drug use (Downs, 1985; Frajzyngier et al., 2007).

Recently, investigators have argued for the expanded use of quantitative analyses of behavior to isolate potential mechanisms that may be responsible for drug effects (Pitts, 2014). Drug self-administration is particularly suited to such quantitative analysis and this may be accomplished through the use of procedures borrowed from economics.

* Corresponding author at: Department of Psychology, Davidson, NC 28035-7037, USA.
E-mail address: masmith@davidson.edu (M.A. Smith).

http://dx.doi.org/10.1016/j.drugalcdep.2017.03.027
Received 20 December 2016; Received in revised form 3 February 2017; Accepted 10 March 2017
Available online 24 May 2017

For instance, using an econometric analysis, the influence of both the intensity of drug demand (i.e., the consumption of the drug when it is free) and the elasticity of drug demand (i.e., how rapidly consumption decreases when the price increases) may be examined. We previously reported that social housing influences cocaine self-administration in male rats by altering the intensity of cocaine demand but not the elasticity of cocaine demand (Peitz et al., 2013), but these findings have not been extended to females. Males and females often differ in their patterns of drug intake (Lynch et al., 2002), suggesting that the behavioral mechanisms influencing cocaine intake may not be the same for both sexes.

Clinical studies indicate that females are more vulnerable to substance use disorders than males and that this may be attributed to gonadal hormones. Indeed, females initiate cocaine use sooner, take less time to become addicted to cocaine, opioids, and alcohol after initial use, and are at a greater risk for relapse following abstinence compared to males (Becker and Hu, 2008; Lex, 1991). In females, drug-seeking behavior differs across the menstrual cycle in primates (human and non-human) and estrous cycle in rodents (Lynch et al., 2000; Newman et al., 2006; Sofuoglu et al., 1999). For example, women reported increased subjective ratings of euphoria and craving following administration of amphetamine and smoked cocaine during the follicular phase of the menstrual cycle compared to the luteal phase (Evans and Foltin, 2006; Evans et al., 2002; Justice and de Wit, 1999; White et al., 2002). Similarly, studies in rodents found that relative to non-estrus females, female rats in estrus reached higher cocaine breakpoints (Hecht et al., 1999; Roberts et al., 1989) and displayed greater responding during extinction and cocaine-primed reinstatement (Feltenstein and See, 2007). These studies provide evidence that fluctuating ovarian hormones influence the subjective effects and self-administration of cocaine and other stimulants, but it is not known how these hormones influence the effects of social contact on drug intake.

The primary aim of the present study was to determine if social contact influences cocaine self-administration in female rats. Female rats were assigned to either isolated or pair-housed conditions in which a social partner either had access to cocaine or did not have access to cocaine. We predicted that cocaine intake would be greatest in rats that had a partner with access to cocaine and least in rats that had a partner without access to cocaine. To determine the mechanisms by which social contact influences cocaine intake we performed an econometric analysis on the dose-response data to see if changes in drug intake were due to changes in the intensity or elasticity of cocaine demand. We also tracked the estrous cycle to determine if estrous moderates the effects of social contact on drug self-administration.

2. Materials and methods

2.1. Subjects

Female, Long-Evans rats were obtained at weaning (~21 days) and randomly assigned to isolated or socially housed conditions upon arrival and placed in polycarbonate “shoebox” cages (interior dimensions: 50 × 28 × 20 cm) for six weeks. After six weeks, rats were transferred to custom-built, operant conditioning chambers that served as home cages for the remainder of the study (see description below). Isolated subjects (n = 13) were housed individually without a social partner. Socially housed rats were subdivided randomly into two groups: in one group (n = 10), subjects were housed with a social partner with access to cocaine (cocaine partner); in the other group, subjects (n = 10) were housed with a social partner that did not have access to cocaine (abstinent partner). Food and water were freely available in the home cages except during the brief period of lever press training (see below). Throughout the study, subjects were maintained on a 12-h light/dark cycle (lights on: 0500) in a temperature- and humidity-controlled colony room. All subjects were maintained in accordance with the guidelines of the Animal Care and Use Committee of Davidson College.

2.2. Apparatus

Rats were trained to lever press using food reinforcement in commercially available operant conditioning chambers (Med Associates Inc., St. Albans, VT). Each chamber was equipped with a single houselight, two response levers, and a food hopper. Experimental events were programmed and data were collected with software and interfacing from Med Associates, Inc. (St. Alban, VT, USA).

All drug self-administration sessions took place in operant conditioning chambers custom made by Faircloth Machine Shop (Winston-Salem, NC, USA). These chambers were IACUC-approved for the long-term housing of rats and served as home cages throughout the period of behavioral testing. Chambers for isolated rats consisted of one 30 × 30 × 30 cm chamber constructed with stainless steel and aluminum. Chambers for pair-housed rats were constructed from two chambers, each with one sidewall removed, and connected with a wire screen. The wire screen permitted rats full visual, auditory, olfactory, and limited tactile contact, but prevented one rat from accessing the response lever and infusion lines of its partner. Each chamber was equipped with one retractable response lever and an infusion pump mounted outside the chamber. Drug infusions were delivered through a Tygon tube protected by a stainless steel spring and attached to a counterbalanced swivel at the top of the chamber. Response levers, syringe pumps, interfacing, and computer software were obtained from Med Associates, Inc. Foam insulation panels (2.5 cm thickness) were placed between chambers to attenuate extraneous sounds and prevent a direct line of sight to other rats in the colony (for further description and images, see Lacy et al., 2014b; Smith, 2012)

2.3. Lever-press training

Five weeks after arrival and one week prior to catheter implantation, rats were lightly food restricted to no less than 90% of their free-feeding body weight and trained to press a response lever on a fixed ratio (FR1) schedule of food reinforcement. On this schedule, each response produced a 45 mg food pellet delivered to a food hopper located between the two response levers. Sessions terminated automatically once 40 reinforcers were delivered or 2 h elapsed, whichever occurred first. Training continued in this manner until a rat earned the maximum number of reinforcers over four days.

2.4. Estrous cycle monitoring

Concurrent with the beginning of lever press training, daily collection of vaginal cells (via lavage) began in female subjects. Samples were collected and analyzed using light microscopy (×100) less than 1 h before each self-administration session. The cells were categorized into one of four estrous phases: metaestrus, diestrus, proestrus, and estrus (Goldman et al., 2007; Hubscher et al., 2005; Marcondes et al., 2002).

2.5. Catheter implantation

Rats were anesthetized with a combination of ketamine (100 mg/kg, ip) and xylazine (15 mg/kg, ip) and a catheter was implanted in the right jugular vein and exited on the dorsal surface between the scapulae (Lacy et al., 2014a; Smith et al., 2008). Ketoprofen (3.0 mg/kg, sc) was given immediately after surgery as a post-operative analgesic and again 24 h later. Beginning on the day of surgery, a solution of heparinized saline and ticarcillin (20 mg/kg, iv) was infused through the catheter daily to prevent infection and maintain patency. After seven days, ticarcillin was discontinued and only heparinized saline was used to maintain catheter patency. Wounds were treated with a topical antibiotic ointment for two days after surgery. All animals were allowed to recover for at least three days before beginning self-administration