Published in final edited form as:
Drug Alcohol Depend. 2014 August 1; 141: 1–8. doi:10.1016/j.drugalcdep.2014.04.025.

The Effects of Social Learning on the Acquisition of Cocaine Self-Administration

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Abstract

Background—Social learning models of substance use propose that drug-use behaviors are learned by observing and mimicking the behavior of others. The aim of this study was to examine the acquisition of cocaine self-administration in three groups of experimentally naïve rats: rats that were tested in isolation, rats that were tested in the presence of another rat that had access to cocaine and had previously been trained to self-administer cocaine, and rats that were tested in the presence of another rat that did not have access to cocaine.

Methods—Male rats were reared in isolated or pair-housed conditions and implanted with intravenous catheters. Pair-housed rats were then assigned to drug-experienced or drug-naïve conditions. In the drug-experienced condition, one rat of each pair was trained to self-administer cocaine in isolation before the reintroduction of its partner. In the drug-naïve condition, one rat of each pair did not have access to cocaine for the duration of the study. For each group, the acquisition of cocaine self-administration was measured over 15 days in rats with access to cocaine but no prior operant training.

Results—Rats tested with a drug-experienced partner were faster to acquire cocaine self-administration and emitted more active lever presses than rats tested with a cocaine-naïve partner. Data for the isolated control group fell between the other two groups on these measures.

Conclusion—These data indicate that the acquisition of cocaine self-administration can either be facilitated or inhibited by social contact. Collectively, these results support a social-learning model of substance use.

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Author Disclosures

Contributors
Mark Smith conceived of the study and wrote the manuscript. Ryan Lacy and Justin Strickland contributed to the experimental design, collected data, and edited the final draft of the manuscript. All authors read and approved the final draft of the manuscript.

Conflict of Interest
The authors have no financial conflicts of interest in regard to this research.

Keywords

cocaine; rat; self-administration; social; social learning

1. INTRODUCTION

Social learning models of substance use propose that drug use is learned, in part, by observing and mimicking the behavior of others (see reviews by Andrews and Hops, 2010; Kandel, 1986; Pandina et al., 2010). Despite the popularity of these models, very few experimental studies have examined the role of social learning in drug use, possibly due to a lack of animal models that allow subjects to observe and mimic the drug use behavior of another subject. We recently described the use of custom-built, operant conditioning chambers that permit two rats to be tested simultaneously during periods of intravenous, drug self-administration (Smith, 2012). Using these chambers, we reported that cocaine self-administration could either be increased or decreased based on the behavior of a partner. Specifically, we reported that cocaine self-administration was facilitated when a rat was paired with another rat with simultaneous access to cocaine, but cocaine self-administration was inhibited when a rat was paired with another rat without access to cocaine. Such data support a social learning model by showing that the behavior of a peer, as opposed to merely the presence of a peer, determines whether social contact increases or decreases drug self-administration.

In our previous study, all rats received lever-press training using food reinforcement before self-administration testing, and this prevented us from examining the role of social learning on the acquisition of drug self-administration. This is relevant because a rapid transition from initial drug exposure to regular patterns of use is an important prognosticator of whether an individual will later develop problems with substance use (U.S. Congress, Office of Technology Assessment, 1994). The acquisition of regular patterns of intake after initial drug exposure is often modeled in the laboratory by exposing a subject to noncontingent drug infusions and then permitting the subject to self-administer that drug during free-operant test sessions. Importantly, factors that increase the rate of acquisition in the laboratory are considered to be risk factors for developing problems with substance use in humans, whereas factors that decrease the rate of acquisition in the laboratory are considered to be protective against substance abuse in humans. For example, social isolation (Kosten et al., 2000) and social stress (Tidey and Miczek, 1997) reliably increase the rate of acquisition in laboratory animals and serve as risk factors in human populations (Chartier et al., 2010; Dube et al., 2006). In contrast, access to alternative, nondrug reinforcers decreases the rate of acquisition in laboratory animals (Carroll and Lac, 1993; Cosgrove et al., 2002), and access to nondrug social activities decreases the acquisition of drug and alcohol use in human adolescents (D'Amico et al., 2012; St. Pierre et al., 1992; for similar studies using the conditioned place preference procedure, see Bahi, 2013; Geuzaine and Tirelli, 2014; Ribeiro Do Couto et al., 2009). To date, the role of social learning in the acquisition of drug self-administration, at least in regard to intravenous drug self-administration, has not been examined.

The purpose of the present study was to examine the contribution of social learning to the establishment of stable patterns of drug intake after initial drug exposure. To this end, the acquisition of cocaine self-administration was examined in three groups of experimentally naïve rats: (1) rats that were tested in isolation, (2) rats that were tested in the presence of another rat that had access to cocaine and had previously been trained to self-administer cocaine (drug-experienced), and (3) rats that were tested in the presence of another rat that did not have access to cocaine (drug-naïve). Behavioral testing advanced through three stages designed to systematically increase the probability that self-administration would be acquired. In phase 1 (days 1–5), responding was reinforced with 0.25 mg/kg cocaine; in phase 2 (days 6–10), responding was reinforced with 0.75 mg/kg cocaine; and in phase 3 (days 11–15), responding was reinforced with 1.5 mg/kg cocaine. Our previous data (Smith, 2012) suggested that cocaine self-administration is enhanced in socially housed rats if both members of the pair have access to cocaine, but cocaine self-administration is inhibited if only one member of the pair has access to cocaine. Consequently, we hypothesized that the rate of acquisition would occur most rapidly in the drug-experienced group and most slowly in the drug-naïve group.

2. METHOD

2.1Animals and Apparatus

Male, Long-Evans rats were obtained at weaning (~21 days) from Charles River Laboratories and assigned to isolated or pair-housed conditions. Both isolated and pair-housed rats were housed in standard laboratory cages (interior dimensions: 50 × 28 × 20 cm) until the beginning of self-administration testing. At that time, all rats were transferred to custom-built, operant conditioning chambers that served as home cages for the remainder of the study. All rats were kept in a temperature- and humidity-controlled colony room on a 12 hr light/dark cycle (lights on: 0500) for the duration of the study. All animals were maintained in accordance with The Guide for Care of Laboratory Animals (Institute of Laboratory Animals Resources, 2011).

All drug self-administration sessions were conducted in custom-built, operant conditioning chambers described previously (Smith, 2012). Briefly, chambers for isolated rats were cubic in design with two response levers on the rear wall. Chambers for pair-housed rats were constructed from two isolated chambers separated by a 14-gauge wire-screen panel. The wire screen allowed pair-housed rats visual, auditory, olfactory, and limited tactile contact with each other, but prevented one rat from accessing the tethering system of its companion. Each rat had individual access to two response levers mounted on the rear wall. The response levers were positioned 13 cm apart and 6 cm from each sidewall. For pair-housed rats with access to cocaine, the inner lever (i.e., the lever in closest physical proximity to the partner) was designated the active lever, whereas the outer lever was designated the inactive lever. Drug infusions were delivered via Tygon tubing protected by a stainless steel spring and connected to a counter balanced swivel suspended above the chamber. An infusion pump (3.33 rpm) was mounted behind the cage and connected to interfacing equipment provided by Med Associates, Inc. (St Albans, VT, USA). Fresh food was placed inside the cages daily, and water dispensers were continuously available inside the cage.

Lever-press training for cocaine-experienced rats (see below) was conducted in standard, commercially available, operant conditioning chambers from Med Associates, Inc. These chambers were equipped with two response levers, two white stimulus lights above the response levers, a house light, and a food pellet receptacle located between the two response levers.

2.2 Group Assignments

Isolated rats were housed individually and tested in individual test chambers with no visual contact with other rats. Pair-housed rats were randomly assigned to cocaine-experienced and cocaine-naïve groups approximately five weeks after arrival. Rats in the isolated and cocaine-naïve groups remained undisturbed in their home cage until surgery and catheter implantation.

For rats in the cocaine-experienced group, one rat of each pair (the cocaine-experienced rat) was trained to press a lever using food reinforcement. Approximately five weeks after arrival, these rats were food restricted to no less than 90% of their free-feeding body weight, placed in operant conditioning chambers, and trained to press a response lever on a fixed ratio (FR1) schedule of reinforcement. Training sessions lasted 2 hr or until 40 reinforcers were delivered, whichever occurred first. Daily training sessions continued in this manner until a rat received the maximum number of 40 reinforcers during any four training sessions. Once this criterion was met, training was discontinued and the rat was placed back on unrestricted feed. The experimentally naïve partners of the cocaine-experienced rats were left undisturbed in the home cage throughout this time period.

Cocaine-experienced rats were surgically implanted with intravenous catheters six weeks after arrival and five days before their experimentally naïve partners (see below). Three days after surgery, cocaine-experienced rats were placed in custom-built, operant conditioning chambers (in isolation and without their experimentally naïve partner) during daily training sessions. Each session began with a priming infusion of cocaine, and the insertion of two retractable levers into the home cage. Each response on the inner (active) lever produced an infusion of cocaine and retraction of the lever for 20 s. All infusions, including the priming infusion, delivered 0.5 mg/kg cocaine over a duration of 2.5–3.0 seconds (based on body weight). Each session lasted 2 hr with no limit placed on the maximum number of infusions that could be earned. Training continued in this manner for 5 consecutive days, at which time the cocaine-experienced rats were joined by their experimentally naïve partners during daily test sessions (see below).

Rats that lost catheter patency before the end of testing were removed from the study and not included in the statistical analysis. For socially housed rats, if one member of the pair lost catheter patency before the end of testing, then both members of the pair were removed from the study and not included in the statistical analysis. This practice led to the removal of a greater number of socially housed rats than isolated rats from the study (rats removed: n = 1 experimentally naïve isolated rat; n = 5 cocaine-experienced rats and their 5 experimentally naïve partners; n = 3 cocaine-naïve rats and their 3 experimentally naïve partners). A total of 62 rats completed all phases of testing (n = 24 experimentally naïve isolated rats; n = 9 cocaine-experienced rats and their 9 experimentally naïve partners; n =

10 cocaine-naïve rats and their 10 experimentally naïve partners). All data (e.g., % of rats meeting the acquisition criterion) reflect only those animals that completed all phases of the study.

2.3 Surgery

All rats were surgically implanted with intravenous catheters between six and seven weeks after arrival. Rats were deeply anesthetized with a combination of ketamine HCL (100 mg/kg, ip) and xylazine HCl (8.0 mg/kg, ip). An intravenous catheter was implanted into the right jugular vein and exited the body via a port implanted on the dorsal surface of the scapulae. Ketoprofen (3.0 mg/kg, sc) was given immediately after surgery as an analgesic, and a solution of heparinized saline and ticarcillin (20 mg/kg, iv) was infused through the catheter daily for 7 days to maintain patency and prevent infection. After 7 days, ticarcillin was discontinued and only heparinized saline was used to maintain catheter patency. All rats were allowed to recover for three days before beginning acquisition testing. We employ a three-day recovery period because general indices of health and behavioral activity (e.g., feeding, drinking, wheel running) return to pre-surgical levels within three days using our surgical protocol.

2.4 Acquisition of Cocaine Self-Administration

Immediately prior to the beginning of acquisition testing, all rats were transferred to the custom-built, operant conditioning chambers, which served as home cages for the remainder of the study. All cocaine self-administration sessions began promptly at the beginning of the dark phase of the light/dark cycle (lights off: 1700).

All rats in the isolated group, all experimentally naïve rats in the cocaine-experienced group, and one member of each pair of the cocaine-naïve group were tested for the acquisition of cocaine self-administration. Each session began with the insertion of two retractable levers into the chamber and a noncontingent infusion of cocaine. During all sessions, responding was reinforced on a FR1 schedule of reinforcement. On this schedule, each response on the active (inner) lever produced an infusion of cocaine and retraction of the response lever for 20 s to signal a timeout during which cocaine was not available. For all sessions, responses on the inactive (outer) lever were recorded but had no programmed consequences. Sessions lasted 2 hr, with no limit placed on the maximum number of infusions that could be earned. One session was conducted each day for 15 consecutive days.

One member of each pair of the cocaine-naïve group was randomly assigned to be cocaine naïve and did not have access to cocaine for the duration of the experiment. Cocaine naïve rats were implanted with catheters, flushed daily with heparinized saline, and connected to Tygon tubing in the operant conditioning chambers. For these rats, both levers were inactive, and responding had no programmed consequences. Cocaine-experienced rats (i.e., those rats that received prior lever-press training and cocaine self-administration training) were tested with cocaine in the exact same manner as their experimentally naïve partners.

Acquisition testing advanced through three consecutive, five-day phases. During the first phase, (days 1–5), each infusion, including the priming infusion, delivered 0.25 mg/kg cocaine. During the second phase (days 6–10), each infusion, including the priming

infusion, delivered 0.75 mg/kg cocaine. During the third phase (days 11–15), each infusion, including the priming infusion, delivered 1.5 mg/kg cocaine. Progression through the three stages was the same for all rats with access to cocaine, regardless of when they acquired cocaine self-administration.

Acquisition was operationally defined as obtaining a minimum of 8 infusions on each of two consecutive days, with the first of those days marking the date of acquisition. Thus, it was possible for a rat to meet the acquisition criterion on the first day, provided that at least 8 infusions were obtained on both the first and second day of testing. Any rat that obtained a minimum of 8 infusions for the first time on the 15^{th} day received one additional test day. If a rat obtained at least 8 infusions on the 16^{th} day, then it was considered to have met the acquisition criterion on the 15^{th} day.

2.5 Data Analysis

Total active lever presses and total inactive lever presses were compared across experimentally naïve rats from the three groups via one-factor ANOVA. Active and inactive lever presses were also compared across experimentally naïve rats from the three groups using mixed-factor ANOVA, with group serving as the between-subjects factor and dose and day serving as within-subjects factors. Time to acquisition was compared across groups using the non-parametric Kruskal-Wallis test, followed by the Mann-Whitney U-test for planned comparisons. All post-hoc tests were conducted using the Bonferroni adjustment for multiple comparisons.

Additional tests were conducted in pair-housed rats to compare experimentally naïve rats with their cocaine-experienced or cocaine-naïve partners (the study was not powered to perform simultaneous comparisons between all five possible groups). The total number of active lever presses were compared between cocaine-experienced rats and their experimentally naïve partners, and between cocaine-naïve rats and their experimentally naïve partners, using independent-samples t-tests. Active lever presses were also compared via mixed-factor ANOVA, with group serving as the between-subjects factor and dose and day serving as within-subjects factors. For cocaine-naïve rats, the inner lever was arbitrarily defined as the “active” lever.

3. RESULTS

The percentage of rats acquiring cocaine self-administration differed across the three groups on all 15 days of testing, with the cocaine-experienced group having the greatest percentage and the cocaine-naïve group having the lowest percentage (Figure 1A). The three groups also differed in the rate at which they acquired cocaine self-administration [Figure 1B; $\chi^2(2, N = 43) = 6.94$, $p = .031$], with rats from the cocaine-experienced group acquiring significantly faster than rats from the cocaine-naïve group ($p = .012$). The number of active lever presses increased in all three groups across the 15 days of testing [Figure 1C; main effect of dose: $F(2, 80) = 10.594$, $p < .001$; main effect of day: $F(4, 160) = 12.193$, $p < .001$], and differed significantly across groups [main effect of group: $F(2, 40) = 3.306$, $p = .047$]. When only the total number of active lever presses was considered, the cocaine-experienced group emitted significantly more active lever presses than the cocaine-naïve

group (Figure 1D; $p = .047$). In contrast, the number of inactive lever presses did not vary significantly across the 15 days of testing [no main effect of dose or day; Figure 1E], but significant group effects were observed [$F(2, 40) = 4.459$, $p = .018$]. When only the total number of inactive lever presses was considered, the isolated group emitted significantly more inactive lever presses than the cocaine-naïve group (Figure 1F; $p = .014$).

The maintenance of cocaine self-administration was examined by comparing the number of infusions obtained on day 15 across the three groups using only data from rats that met the acquisition criterion. In the 5 cocaine-naïve rats, 19 isolated rats, and 8 cocaine-experienced rats meeting the acquisition criterion, cocaine self-administration did not differ across the three groups (Figure 2). Analysis of individual event records revealed stable response patterns with regular post-reinforcement pauses in the majority of animals (data not shown).

Cocaine-experienced rats in the cocaine-experienced group exhibited high levels of responding on the first day of testing (Figure 3A). As expected, the number of infusions decreased in these rats as the dose of cocaine increased. In contrast, only increases in responding were observed in their experimentally naïve partners over the 15 days of testing, resulting in significant differences between the two groups during early but not later stages of testing [dose × group interaction: $F(2, 32) = 10.832$, $p < .001$]. When data from all 15 days were considered, cocaine-experienced rats emitted significantly more total active lever presses than their experimentally naïve partners [Figure 3B; $t(16) = 2.626$, $p = .018$].

Cocaine-naïve rats and their experimentally naïve partners exhibited low levels of responding that increased significantly, albeit slowly, over the 15 days of testing (Figure 4A; main effect of dose: $F(2, 36) = 4.343$, $p = .020$; main effect of day: $F(4, 72) = 3.922$, $p = .006$). Although numerically greater levels of responding were observed in rats with access to cocaine by the end of the testing period, no significant main effect of group or significant interaction was observed. Similarly, no differences were observed between cocaine naïve rats and their experimentally naïve partner in the total number of “active” lever presses (Figure 4B).

4. DISCUSSION

The principal finding of this study is that the behavior of a peer, as opposed to merely the presence of a peer, determines whether the acquisition of cocaine self-administration will be increased or decreased by social contact. In the present study, experimentally naïve rats paired with a cocaine-experienced partner met the acquisition criterion twice as quickly (6 vs. 12 days) than experimentally naïve rats paired with a cocaine-naïve partner. Furthermore, rats paired with a cocaine-experienced partner emitted approximately 150 more active lever presses (231 vs. 84 responses) than rats paired with a cocaine-naïve partner. These differences were substantially greater than the differences observed in the number of inactive lever presses (90 vs. 45 responses), which failed to reach statistical significance between these groups. Importantly, these differences could not be attributed to differences in sensitivity to cocaine. When only rats meeting the acquisition criterion were compared on the final day of testing, cocaine self-administration did not differ between the three groups.

There is not a standardized procedure for measuring the acquisition of drug self-administration in laboratory animals, but many studies include noncontingent infusions of the drug at the onset of testing, either through priming infusions or autoshaping procedures, and then permit the animal to respond for contingent infusions of the drug under free-operant conditions (e.g., Campbell and Carroll, 2000; Carroll and Lac, 1993; Perry et al., 2005; Roth and Carroll, 2004; Schenk et al., 2001; Smith and Pitts, 2011; Soria et al., 2006). This method is considered to model human patterns of acquisition in which a drug is initially provided freely (such as by a friend or a dealer), and then the monetary or behavioral costs of obtaining the drug increase as the individual shifts to regular patterns of use (see review and discussion by Carroll and Meisch, 2011). It must be noted that noncontingent infusions are not necessary for the acquisition of drug self-administration, and many studies describe the acquisition of responding in the absence of priming infusions or autoshaping procedures (e.g., Belluzi et al., 2005; Bird and Schenk, 2013; Crombag et al., 2008; Kabbaj et al., 2001; Schippers et al., 2012). Moreover, such procedures model the acquisition of drug self-administration under conditions in which drugs are available only after a monetary or behavioral price has been paid (e.g., paying for the drug, exchanging services for the drug, or traveling to a location to procure the drug).

Studies with animals have consistently shown that increasing the dose of the drug increases the likelihood that self-administration will be acquired (Campbell et al., 1998; Carroll and Lac, 1997). In the present study, behavioral testing advanced through three distinct phases in which the dose of cocaine was systematically increased. Importantly, these phases were not designed to measure the impact of increasing doses of cocaine on acquisition; rather, they were designed to progressively increase the likelihood that self-administration would be acquired. Consistent with this aim, the percentage of rats acquiring self-administration progressively increased across all three phases of testing. As noted above, differences between groups were apparent during each of these phases.

Our experimental chambers are constructed so that the active levers for socially housed rats are in close physical proximity to their partners. This is done to maximize the effects of social learning in acquiring the response, given that previous studies have indicated that social learning is enhanced if the model and observer are in close physical proximity (Aisner and Terkel, 1992; Coussi-Korbel and Fragaszy, 1995; Hausberger et al., 1995). It is important to note that we did not see evidence that rats were inadvertently pressing the active lever by trying to interact with their partner, because there was no preference for the active versus inactive lever in the early days of testing prior to the acquisition of drug self-administration, nor was there a preference for one lever or the other in cocaine naïve rats that never received cocaine.

Experimentally naïve rats paired with cocaine-experienced rats were the fastest to acquire cocaine self-administration and emitted the most active lever presses over the 15-day testing period. Decades of research in social learning have uncovered a number of behavioral mechanisms that may account for the rapid acquisition of cocaine self-administration in this group of animals. A popular explanation that is often found in social learning models of substance use proposes that drug-use behaviors are acquired by observing and imitating the drug use behaviors of others (Kandel, 1985). Imitation could account for the elevated levels

of responding and subsequent faster rates of acquisition in these rats because their cocaine-experienced partners exhibited high rates of active lever pressing throughout the duration of testing. As an alternative explanation, social facilitation is a process by which responding is increased by the presence of another individual. For instance, alcohol self-administration is facilitated in prairie voles housed with a same-sex sibling compared to those housed in isolation (Hostetler et al., 2012). Importantly, social facilitation is greatest if both individuals are performing the same behavior (Hake and Laws, 1967). In the present study, only experimentally naïve rats in the cocaine-experienced group were paired with other rats that were engaged in cocaine self-administration, and social facilitation would be expected to be greatest in this group. Finally, stimulus enhancement is a process by which one individual directs the attention of another to a specific stimulus in the environment that is associated with reinforcement. For example, rats acquire nicotine self-administration at a faster and greater rate in the presence of a demonstrator that is drinking a scented solution associated with nicotine reinforcement; however, this effect is abolished if the demonstrator is drinking a scented solution that is not associated with nicotine reinforcement (Chen et al., 2011). In the present study, cocaine-experienced rats emitted high levels of responding on the active response lever, which likely increased the salience of the active lever for their experimentally naïve partners. It should be noted that these explanations are not mutually exclusive of one another, and all likely contributed to the elevated levels of responding and faster rates of acquisition in these rats.

Experimentally naïve rats paired with cocaine-naïve rats were the slowest to acquire cocaine self-administration and emitted the fewest lever presses over the 15-day testing period. These data are consistent with studies reporting social housing in the home cages decreases rates of drug self-administration (Gipson et al., 2011), and slows the acquisition of cocaine self-administration (Howes et al., 2000). Environmental enrichment provided by social housing could account for the lower rates of active lever pressing and acquisition of cocaine self-administration in this group. Numerous studies have reported that environmental enrichment produces functional changes in dopamine binding proteins (Del Arco et al., 2007; Gomez et al., 2012; Zhu et al., 2004), alters sensitivity to direct and indirect dopamine agonists (Del Arco et al., 2007; Hoffmann et al., 2009), and decreases amphetamine (Bardo et al., 2001; Green et al., 2002) and cocaine (Puhl et al., 2012, but see Smith et al., 2009) self-administration. Alternatively, the presence of another rat may have served as an alternative, nondrug reinforcer in this group. Many studies have reported that access to an alternative nondrug reward decreases drug-maintained responding (e.g., Comer et al., 1996; Cosgrove et al., 2002; Cosgrove and Carroll, 2003) and slows the acquisition of drug self-administration (e.g., Campbell et al., 1998; Carroll et al., 1989). It must be noted that this effect was only apparent in rats paired with a cocaine-naïve partner that never had access to cocaine, suggesting that a cocaine-experienced (or a cocaine-intoxicated) partner does not serve as an alternative, nondrug reinforcer to decrease cocaine self-administration.

The neurobiological mechanisms responsible for the effects of social learning on drug self-administration are not known, but candidate systems are those that process information regarding both drug and social stimuli (see reviews by Bardo et al., 2013; Burkett and Young, 2012; McGregor and Bowen, 2012). For instance, the amygdaloid complex plays a critical role in the assimilation of interoceptive (i.e., drug effects) and exteroceptive (i.e.,

social environment) stimuli and may serve as a locus of integration for drug and social reinforcement (Badiani, 2013). Alternatively, the nucleus accumbens mediates the positive reinforcing effects of both self-administered drugs and social contact and may serve to mediate the effects of social learning on drug self-administration. Supporting this latter possibility, both oxytocin and dopamine D_2 receptors in the nucleus accumbens are required for the development of social attachment in rodents, and stimulant-induced increases in dopamine concentrations in the nucleus accumbens are attenuated by central administration of oxytocin (Liu and Wang, 2003; Qi et al., 2008).

The present findings are consistent with our previous study reporting that cocaine self-administration is enhanced in socially housed rats if both members of the pair have access to cocaine, but cocaine self-administration is inhibited if only one member of the pair has access to cocaine (Smith, 2012). In our previous study, all rats were trained to press a response lever prior to self-administration training, so there was no opportunity to examine the role of social learning on the acquisition of a novel drug-reinforced response (i.e., all rats responded on the first day in which cocaine was available and received the maximum number of infusions available). Collectively, these studies suggest that social learning plays a role in both the acquisition of drug use and the maintenance of drug use once established.

From a translational perspective, the present findings suggest that social contact with individuals who engage in substance use may accelerate a person's substance use and increase the likelihood that he or she will become a habitual user of drugs. On the other hand, these data also suggest that social contact with individuals who practice abstinence, regardless of reason, may delay an individual's substance use and decrease the odds that he or she will become a regular user of drugs. These results are consistent with epidemiological studies reporting that having friends who use drugs is a risk factor for adolescent drug use (Bahr et al., 2005; Simons-Morton and Chen, 2006; Walden et al., 2004), but that participation in community, religious, and after-school activities is associated with lower rates of adolescent drug use (Brown et al., 2001; D'Amico et al., 2012; Mellor and Freeborn, 2011; St. Pierre et al., 1992; Tebes et al., 2007). Coupled with the present data, such studies argue for the expanded use of socially based interventions in drug abuse prevention programs.

Acknowledgments

The authors thank Maryam Witte and Mary Kathryn Brophy for expert technical assistance, Amy Sullivan for animal care and maintenance, Chris Van Rooyen for instrumentation support, and the National Institute on Drug Abuse for supplying the study drug.

Role of Funding Source

Funding for this study was provided by NIH Grants DA031725 and DA027485; the NIH had no further role in designing the study, collecting the data, interpreting the results, writing the manuscript, or submitting the paper for publication.

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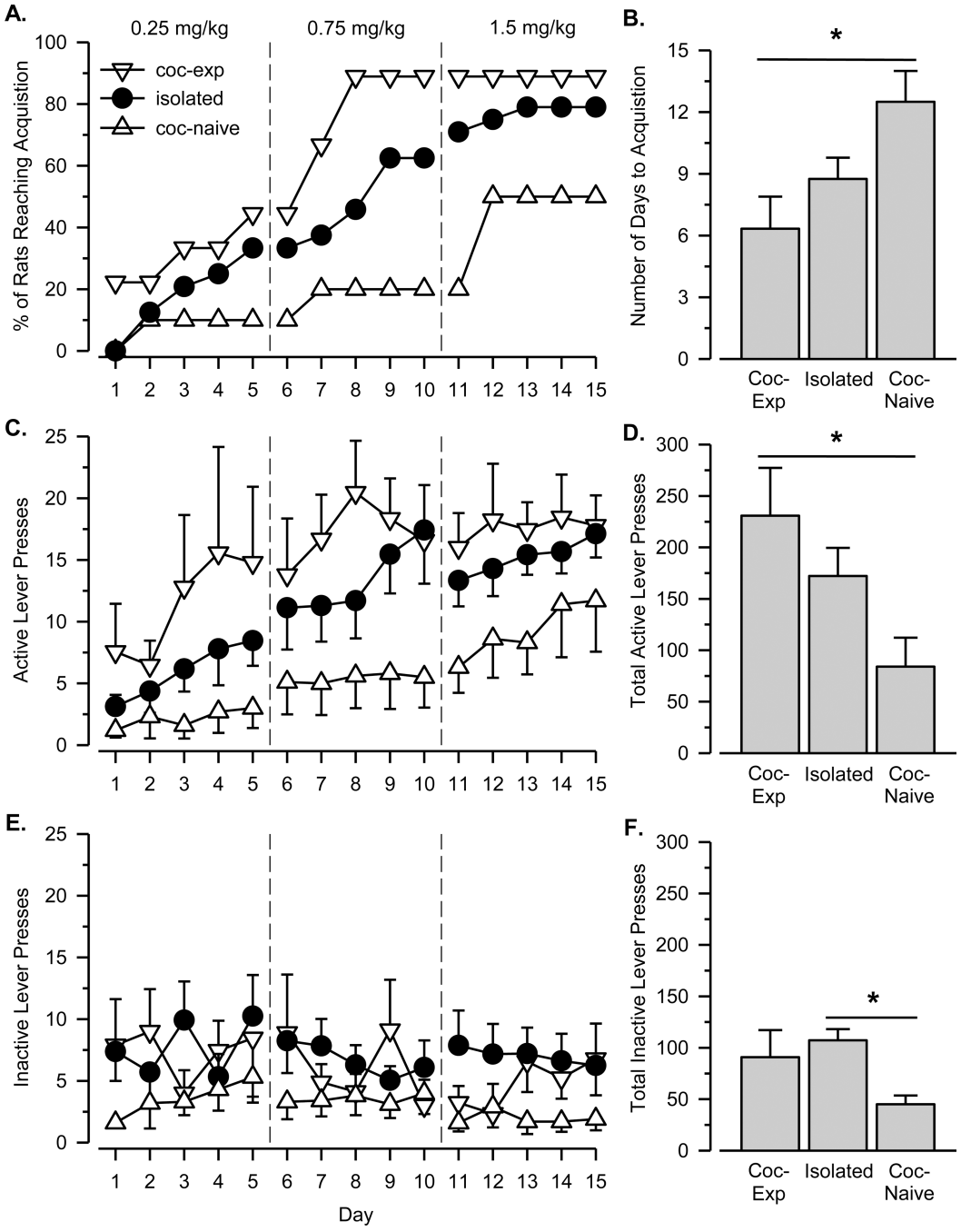

Figure 1.

A. Percent of experimentally naïve rats reaching the acquisition criterion over 15 days of testing in each of the three groups. B. Number of days to reach the acquisition criterion. C. Number of active lever presses per session over 15 days of testing. D. Total number of active lever presses over 15 days of testing. E. Number of inactive lever presses per session over 15 days of testing. F. Total number of inactive lever presses over 15 days of testing. Asterisks (*) indicate significant difference between groups. For panels A, C, and E, vertical reference lines represent transitions between different experimental events: self-

administration testing with 0.25 mg/kg/infusion cocaine (days 1–5); self-administration testing with 0.75 mg/kg/infusion cocaine (days 6–10); self-administration testing with 1.5 mg/kg/infusion cocaine (days 11–15). For all panels, vertical lines surrounding data points represent the SEM; where not indicated, the SEM fell within the data point.

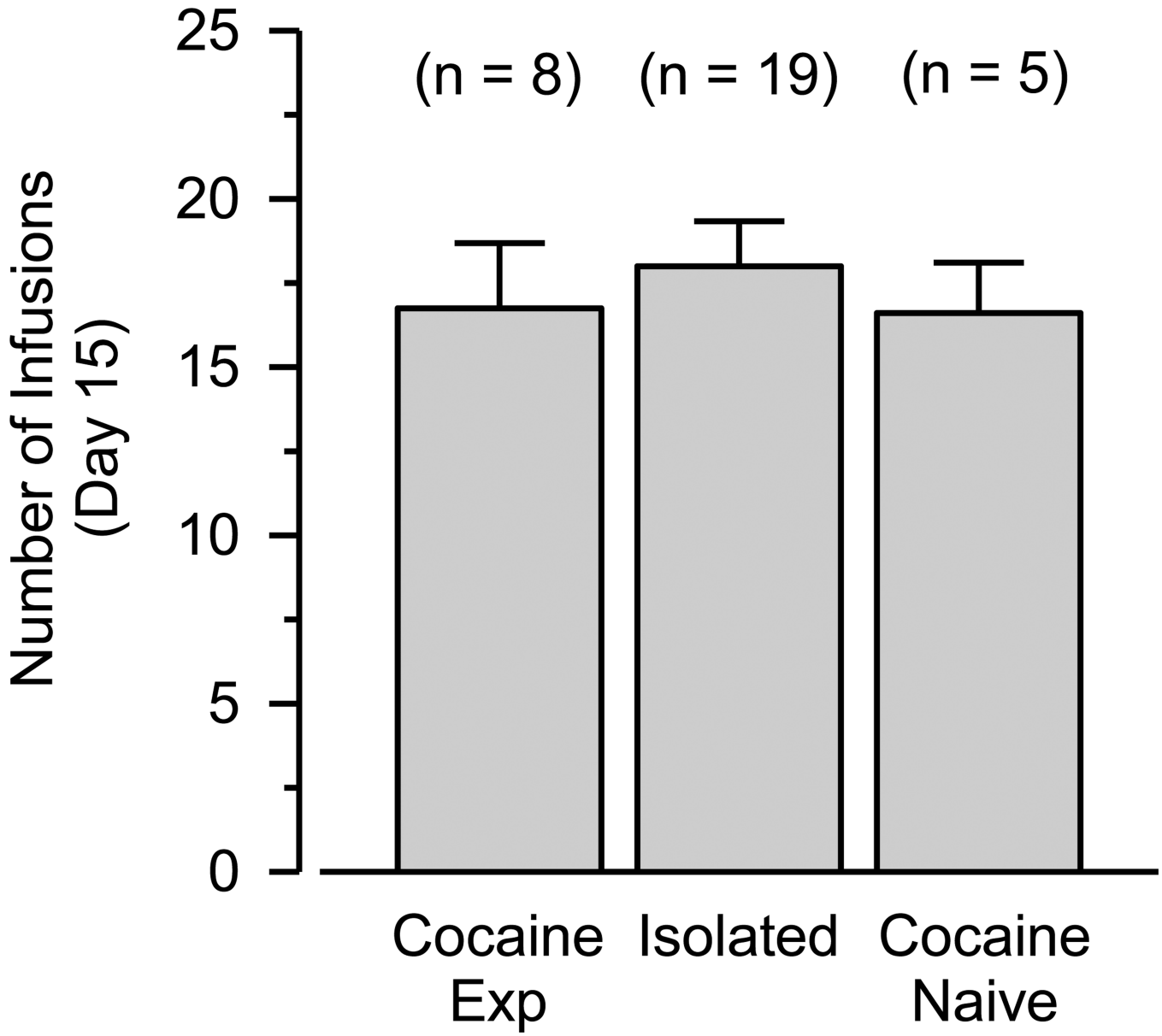

Figure 2.

Cocaine self-administration during the 15th session in only those rats meeting the acquisition criterion. Vertical axis indicates number of infusions during 2-hr test session. Data are shown from 8 experimentally naïve rats from the cocaine-experienced group, 19 experimentally naïve rats from the isolated group, and 5 experimentally naïve rats from the cocaine-naïve group.

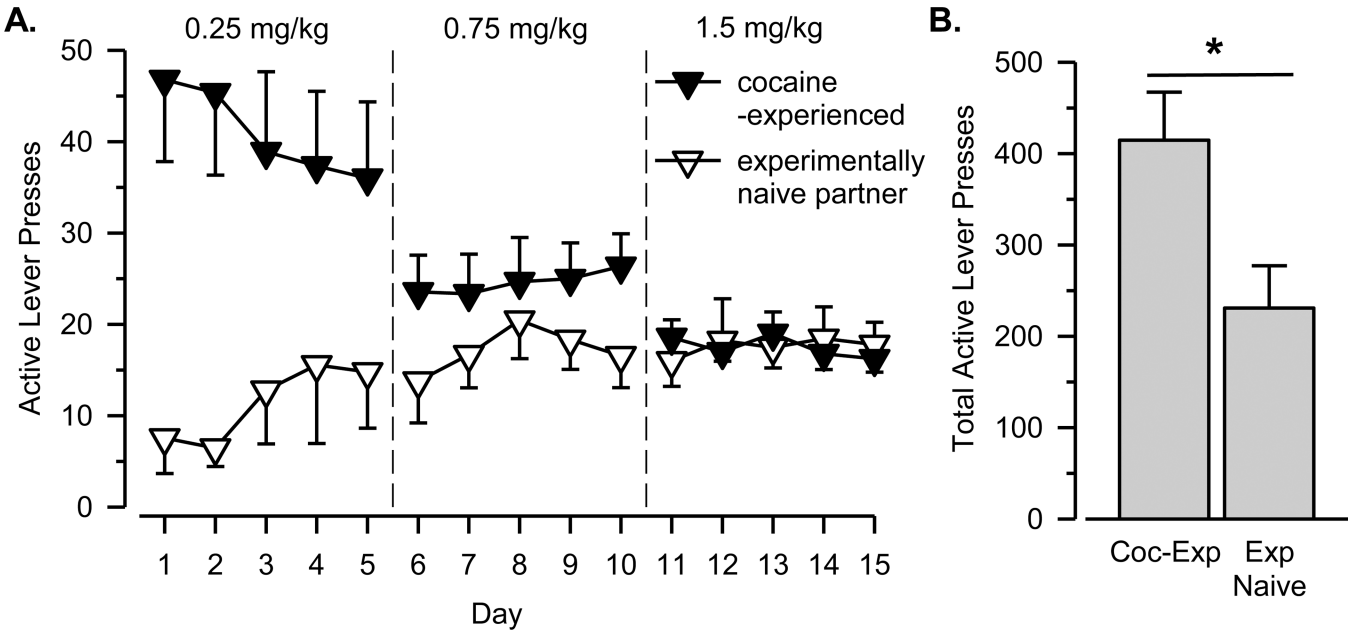

Figure 3.

A. Number of active lever presses per session over 15 days of testing for the cocaine-experienced group. B. Total number of active lever presses over 15 days of testing. Asterisks (*) indicate significant difference between groups. See Figure 1 for additional details.

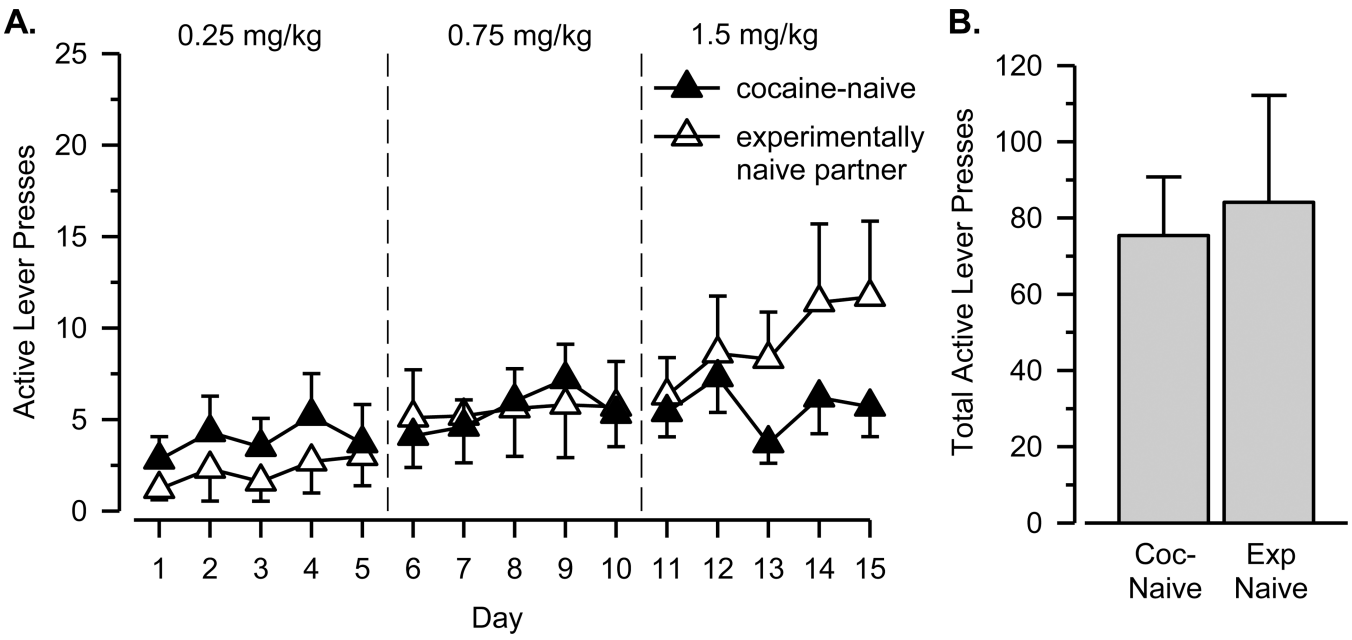

Figure 4.

A. Number of active lever presses per session over 15 days of testing for the cocaine-naïve group. B. Total number of active lever presses over 15 days of testing. See Figure 1 for additional details.