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Mini review Animal models of social contact and drug self-administration

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ABSTRACT

Social learning theories of drug abuse propose that individuals imitate drug use behaviors modeled by social peers, and that these behaviors are selectively reinforced and/or punished depending on group norms. Historical-ly, animal models of social influence have focused on distal factors (i.e., those factors outside the drug-taking context) in drug self-administration studies. Recently, several investigators have developed novel models, or significantly modified existing models, to examine the role of proximal factors (i.e., those factors that are immediately present at the time of drug taking) on measures of drug self-administration. Studies using these newer models have revealed several important conclusions regarding the effects of social learning on drug abuse: 1) the presence of a social partner influences drug self-administration, 2) the behavior of a social partner determines whether social contact will increase or decrease drug intake, and 3) social partners can model and imitate specific patterns of drug self-administration. These findings are congruent with those obtained in the human laboratory, providing support for the cross-species generality and validity of these preclinical models. This minireview describes in detail some of the preclinical animal models used to study social contact and drug self-administration to guide future research on social learning and drug abuse.

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1. Introduction

The social environment plays a critical role in the etiology and persistence of drug use disorders. Many social factors are distal to the drug-taking context and are not immediately present at the time in which drugs are used. These factors include those found in the individual's home, school, and community environments, and these factors may serve to increase or decrease the probability of drug use. Preclinical animal studies have successfully modeled many of these factors and have consistently revealed their role in drug selfadministration. For example, studies using rodents and non-human primates have revealed that social stress and social isolation increase, whereas social enrichment and social dominance decrease, drug selfadministration across a wide variety of drug classes and schedules of reinforcement (see reviews by Burke and Miczek, 2014; Nader et al., 2012; Stairs and Bardo, 2009). That drug use in humans is similarly affected by distal social factors (e.g., Gordon, 2002) supports the validity of these models for predicting human drug use and for evaluating putative interventions for drug use disorders.

Unfortunately, preclinical studies examining proximal social factors (i.e., those factors that are immediately present during the drug-taking event) have not advanced at the same pace. Historically, preclinical

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investigators have been hampered by a relative dearth of models that adequately assess and allow manipulation of proximal social variables. Only recently has the design and validation of models that allow extensive and systematic evaluation of these factors increased. For example, several recent studies have examined the effects of proximal social contact on conditioned drug reward using the conditioned place preference (CPP) procedure. In the CPP procedure, a Pavlovian association is formed between a stimulus (e.g., a social peer, an interoceptive drug cue) and an environmental context, and a preference for the stimuluspaired environment serves as a measure of the rewarding effects of the stimulus. These studies have consistently revealed enhanced rewarding effects when drug and social stimuli are conditioned together (Thiel et al., 2008; Watanabe, 2011). Similarly, when conditioned as mutually exclusive conditions, social contact can compete with the rewarding effects of drug stimuli (Fritz et al., 2011a, 2011b).

Recent research has also begun examining the effects of social contact on drug self-administration, and several recent reviews have described the effects of social contact on various measures of drug intake. These reviews have examined the neurobiological mechanisms at the nexus of social contact and drug self-administration (Bardo et al., 2013), the behavioral mechanisms mediating the effects of social contact on drug self-administration (Strickland and Smith, 2014), the intersection of emotional valance and social context in drug selfadministration (Neisewander et al., 2012), and the effects of social contact on conditioned drug reward (Zernig et al., 2013). The primary objective of this mini-review is to provide an evaluation of several

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preclinical models of proximal social contact and their application to the study of drug self-administration (see Fig. 1 for schematic overview of the described models). To this end, we have identified three key conclusions from this literature and will discuss the models within this context. The collective findings from these studies indicate that: 1) the presence of a social peer influences drug self-administration, 2) the effects of social contact are moderated by the behavior of that peer, and 3) animals can model and imitate specific patterns of drug self-administration.

2. Social learning theories of social contact

One of the strongest prognosticators of adolescent and young adult drug use is the drug-use behavior of peers (Bahr et al., 2005; Walden et al., 2004). A number of epidemiological studies have explored the link between social factors and drug self-administration, and have provided cogent support for the influence of peers (Bot et al., 2005; Kelly et al., 2013; Salvy et al., 2014). The results of this research indicate that peer influence occurs at both a distal (e.g., incorporation of group norms) and proximal (e.g., spending time with others who use drugs) level. Equally important to note is recent evidence suggesting that distal factors become less salient over time while proximal factors become more influential (Salvy et al., 2014). Thus, at the broadest level, peers play a critical role in the expression and continuation of drug use, with proximal influences having a progressively greater impact over time.

Although several theories exist to explain peer influence and the high concordance of drug use among members of peer groups, social learning theories (i.e., group socialization theories) have garnered a great deal of attention. Social learning theories posit that attitudes, beliefs, and behaviors held by a social group are transmitted to individual members, and that social interactions determine future member behavior (Akers, 1977; Kandel, 1986). Further, peers may selectively reinforce desired behaviors (e.g., drug use) and punish undesired behaviors (e.g., drug abstinence) of other group members. The emergence of novel preclinical models of social contact offers a platform by which hypotheses derived from social learning theories can be tested. This is important because social learning theories propose a number of mechanisms by which the social environment can be manipulated to prevent and treat drug use and abuse (see Strickland and Smith, 2014). Thus, the development of preclinical models of social contact has the potential to contribute to the translational design and implementation of interventions for drug use disorders, as well as a broader understanding of the social mechanisms of drug self-administration.



a) *Home-Cage Consumption*: Subjects are given home cage access to drug in social housing (e.g., Alexander et al., 1978)



c) *Prairie Vole Ethanol Consumption*: Uses socially monogamous rodents to examine ethanol consumption in social dyads (e.g., Anacker et al., 2011)



b) Social Access Procedure:

Pairs a social access US with retractable ethanol sipper CS to examine social access effects on ethanol drinking (e.g., Tomie et al., 2004a)



d) *Observer Demonstrator Procedure*: A demonstrator subject is administered an ethanol injection and placed in contact with the observer (e.g., Hunt et al., 2000)

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