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The Impact of Social Interactions and Age on the Reinforcing Properties of Cocaine in Rats

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Introduction

Adolescence is a vulnerable period for drug addiction. Adolescent lab animals have demonstrated an increased sensitivity to cocaine (Brenhouse & Andersen, 2008; Zakharova et al., 2009), methamphetamine (Zakharova et al., 2009), and nicotine (Shram & Lê, 2010; Torres et al., 2008). In addition to being more sensitive to a drug's effects and self-administering it at higher doses, adolescents also are less sensitive to withdrawal symptoms (Schramm-Sapyta et al., 2009). Adolescent drug use by be facilitated by social learning (Akers & Lee, 1996), in which adolescents are socially rewarded for drug use by peer influence, and then come to associate with drug-using peers and social settings, thereby creating a feedback loop. Mice receiving a threshold dose of morphine or amphetamine showed dependence when administered the drug with a drugged conspecific, though not alone or with the partner undrugged (Watanabe, 2011; Watanabe, 2013). This study aimedto further explore the effects of social interaction/context and age on the rewarding properties of cocaine.

Abstract

Conditioned place preference (CPP) experiments have revealed a complex relationship between social interaction, drug dosage, and the hedonic value of drugs. This study explored the variables of age (adolescence versus adulthood) and social context (partnered versus unpartnered) in relation to the reinforcing value of cocaine using the CPP paradigm. Adolescent Sprague-Dawley rats (PND 32-37) were divided into three groups: partnered + saline; unpartnered + cocaine; and partnered + cocaine. Cocaine/partnered was paired with one chamber of the CPP apparatus; saline/unpartnered was paired with the other. Rats (PND 32) underwent a baseline pre-test in the apparatus, in which they were permitted to explore the three chambers for fifteen minutes to determine initial chamber preference. During four days of testing (PND 33-37), rats were injected intraperitoneally with cocaine or saline. If they had a partner rat, the partner rat was injected and placed in the chamber first. Rats were confined to the chamber for thirty minutes following injection. Rats were counterbalanced such that each rat experienced alternating two sessions in their paired chamber and two sessions in their unpaired (control) chamber. On the sixth day (PND 37) the rats underwent a post-test. The procedure from the pre-test was repeated and compartment preference was recorded. It was found that social paired rats displayed conditioned place aversion ($p<.05$) and preferred the control compartment, but when paired with cocaine showed conditioned place preference for the experimental compartment. Both cocaine without social pairing and cocaine with social pairing groups demonstrated CPP ($p<.05$). The finding that the cocaine reversed the social conditioned place aversion suggests that the cocaine changed the hedonic value of the social pairing.

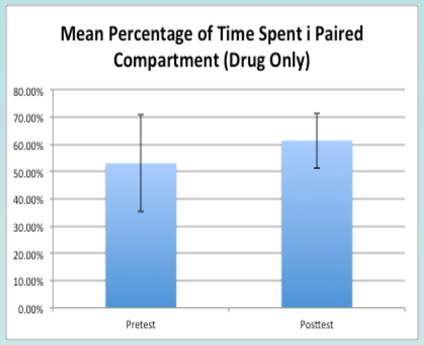
Methods

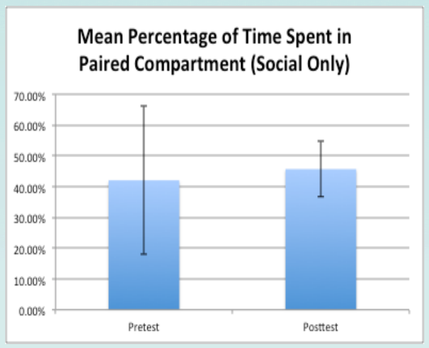
Adolescent rats were divided into three groups (N=10) each: Social Pair, Drug Only, and Social Pair/Drug. In order to measure the hedonistic effects of the drug, this study utilizes the conditioned place preference paradigm (CPP), which through classical conditioning pairs a drug state (UCS) with an environment (CS). The CPP apparatus features two distinct compartments that differ in floor material and wall pattern. Rats underwent a baseline test undrugged in the apparatus in which they were permitted to freely explore all compartments for 15 minutes. Total time spent in each compartment was recorded. On odd days they were confined to one of the two compartments (counterbalanced regardless of baseline compartment preference) while in the presence of an undrugged conspecific (group Social Pair), after receiving an intraperitoneal injection of 2mg/kg cocaine (group Drug Only), or with a conspecific with both rats having received cocaine (group Social Pair/Drug). On even days they were confined to the opposite chamber for 30 minutes while alone (group Social Pair), undrugged (group Drug Only), or alone and undrugged (group Social Pair/Drug). Training continued over four days so that each rat experienced two sessions in each compartment. At test, the rats were again be permitted to freely explore the apparatus undrugged for 15 minutes and time spent in each compartment was recorded. Compartment times at test and at baseline were compared, and significant compartment preference were taken to mean a preference for that compartment's condition during training.

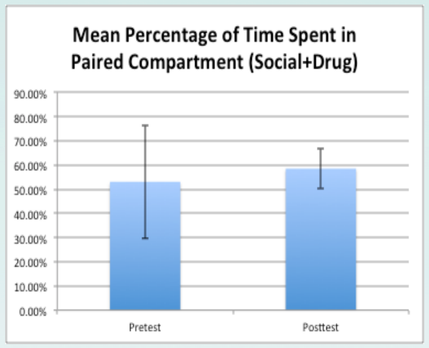
Conclusion

Results of this study mimicked previous findings that adolescents would find a threshold dose of cocaine rewarding, as both drug groups demonstrated CPP. Interestingly, the social pairing group demonstrated conditioned place aversion, as being socially paired proved to have aversive properties than appetitive ones. Previous literature has found that adolescent rats find social interactions more rewarding than adult rats, which would have suggested that being paired wouldn't be aversive. This may be due to housing conditions (rats were housed with their partner rat) or due to dominance/submission dynamics that were not examined in this study. However, this conditioned place aversion effect went away when both rats were drugged, suggesting that the cocaine changed how aversive the social pairing was. Future research would seek to reproduce this conditioned place aversion finding and attempt to isolate if it is because of housing conditions of the temperaments of the rats, as dominance/submission dynamics may play a role in creating dependence, similar to how peer groups are dynamic and not all the same in humans.

Results







Results were analyzed by examining proportion of time (seconds) spent in the non-control compartment (partnered/drugged/partnered and drugged) at baseline versus at test. Rats in the Drug and Drug/Social Pair group both demonstrated CPP at the threshold dose of 2mg/kg ($p>0.05$; $p>0.05$). The Social Pair group demonstrated conditioned place aversion ($p>0.05$) without the presence of the drug while only being paired with an undrugged conspecific..

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