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SHORT COMMUNICATION

Social partners prevent alcohol relapse behavior in prairie voles

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Summary There is robust evidence for a protective role of interpersonal factors such as social support on alcohol relapse, but research on the mechanisms that social factors may be acting on to effectively protect individuals against relapse is lacking. Prairie voles are highly social, monogamous rodents that freely self-administer ethanol in high amounts, and are a useful model for understanding social influences on alcohol drinking. Here we investigated whether prairie voles can be used to model social influences on relapse using the alcohol deprivation effect, in which animals show a transient increase in ethanol drinking following deprivation. In Experiment I, subjects were housed alone during four weeks of 24-h access to 10% ethanol in a two-bottle choice test. Ethanol was then removed from the cage for 72 h. Animals remained in isolation or were then housed with a familiar same-sex social partner, and ethanol access was resumed. Animals that remained isolated showed an increase in ethanol intake relative to pre-deprivation baseline, indicative of relapse-like behavior. However, animals that were socially housed did not show an increase in ethanol intake, and this was independent of whether the social partner also had access to ethanol. Experiment II replicated the alcohol deprivation effect in a separate cohort of isolated animals. These findings demonstrate that prairie voles display an alcohol deprivation effect and suggest a 'social buffering' effect of relapse-like behavior in the prairie vole. This behavioral paradigm provides a novel approach for investigating the behavioral and neurobiological underpinnings of social influences on alcohol relapse.

1. Introduction

Rates of relapse from alcohol use disorders are estimated as high as 80% (Dawson et al., 2007). It is critical to understand the biological mechanisms underlying relapse-related behaviors and to identify target treatments for improving rates of remission in alcoholics. There is robust evidence for a protective role of interpersonal factors such as social support, marital status, and marital quality against alcohol relapse (Garmendia et al., 2008; Walter et al., 2006). However,

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research on the mechanisms that social factors may be acting on to effectively protect individuals against relapse is lacking (Hunter-Reel et al., 2009).

Prairie voles (*Microtus ochrogaster*) are highly social and, unlike other traditional rodent models, show specific social attachments for both same-sex (DeVries et al., 1997) and opposite-sex partners (Carter and Getz, 1993). These animals freely self-administer ethanol in high amounts, and will do so without training on a sucrose-fading procedure (Anacker et al., 2011a). Prairie voles also display drinking patterns under social conditions that contrast with what is typically seen in other animal models. Specifically, voles that are housed in same-sex pairs show higher basal levels of both alcohol consumption and preference compared to animals housed in isolation (Anacker et al., 2011a; Hostetler et al., 2012). This is in contrast to the isolation-induced increases in drinking observed in many other rodents (as reviewed in Anacker and Ryabinin, 2010), and is more similar to social facilitation of drinking that is observed in humans (de Castro, 1990). On the other hand, under certain social conditions, the drinking behavior of one animal can exert a direct and persistent effect to reduce drinking in a social partner (Anacker et al., 2011b). Thus, it is becoming increasingly clear that the details of social context are important factors in the ethanol drinking behavior of voles. This is relevant for modeling human behavior, in which the influence of a social partner can be highly specific to the social relationship and context.

Relapse has been modeled in mice and rats by the alcohol deprivation effect (ADE), in which alcohol-exposed subjects show elevated intake of alcohol following abstinence (Sinclair and Senter, 1968; Spanagel and Holter, 1999). Specifically, animals show a transient (<48 h) increase in alcohol drinking following deprivation. However, mice and rats do not show specific social attachments, and the effects of social influences on the ADE have not been studied in rodents. The aims of this study were two-fold: (1) determine whether prairie voles demonstrate an ADE, and (2) investigate whether the ADE is influenced by the social environment. Specifically, we hypothesized that the presence of a familiar social partner would 'buffer' against expression of the ADE. We also investigated whether the drinking behavior of a social partner would affect the ADE, and expected that a non-drinking ("abstinent") partner would be more effective at social buffering of relapse-like behavior than a drinking partner.

2. Methods

The subjects used in this study were from a breeding colony housed at the Portland Veterans Affairs Medical Center Veterinary Medical Unit. Animals were weaned at 21 days and housed in same-sex sibling groups in cages (27 cm × 27 cm × 13 cm) under controlled temperature, humidity, and 14L:10D light conditions. Food (LabDiet Hi-Fiber Rabbit chow, cracked corn, and oats) and water were available ad libitum throughout the experiments. All subjects had access to cotton nestlets throughout the experiments. All procedures were reviewed and approved by the Institutional Animal Care and Use Committee of the Portland Veterans Affairs Medical Center. Male (n = 36) and female (n = 35) subjects were tested as adults (110—190 days of age at start of testing). Different subjects were used for each experiment.

2.1. Experiment I

All subjects were housed alone in small shoebox cages (27 cm × 16.5 cm × 13 cm) during initial ethanol access and deprivation. Animals had 24 h access to 10% ethanol and tap water in a 2-bottle choice test for 4 weeks (as previously described: Anacker et al., 2011a). On the morning of Day 29, ethanol bottles were removed for a 72-h deprivation period. On Day 32, two groups of animals were placed in mesh-divided housing with a familiar same-sex social partner (Anacker et al., 2011a). Keeping the animals separated allowed individual monitoring of fluid consumption, and the mesh allowed animals to maintain contact and interaction. In one group, the social partners also had access to ethanol ("with drinking partners"; n = 20) and partners in the second group had access to water only ("with abstinent partners"; n = 20). A third group remained isolated in their home cage ("isolated"; n = 19). In social housing conditions, bottles were placed directly on either side of the mesh. Ethanol access was resumed immediately after pairing for an additional 48 h.

Ethanol consumption (g/kg) and ethanol preference (volume ethanol/total fluid consumed) were each analyzed via repeated measures ANOVA with time (baseline, Day 32, and Day 33) as within subject factor and housing (isolated, with drinking partner, or with abstinent partner) as the between subjects factor. A pre-deprivation baseline was calculated from the average of the final 6 days of initial access (Days 23—28; Gilpin et al., 2003). Sex was not a significant factor and was dropped from all models. Post hoc comparisons between baseline and each Day 32 and Day 33 were performed via paired t-tests. To examine whether significant changes in ethanol intake could be explained by changes in total fluid intake (total volume of fluid consumed/weight), total fluid consumption was examined via paired t-tests. Significance was set at $p < 0.05$.

2.2. Experiment II

The second experiment aimed to replicate the ADE in isolated animals seen in Experiment I and to examine ethanol drinking over a longer post-deprivation period. Animals were isolated and had access to 10% ethanol in a 2-bottle choice test as described in Experiment I. In contrast to Experiment I, all 12 subjects remained isolated throughout the study and ethanol access was maintained and monitored for 7 days following deprivation.

For each day post-deprivation, ethanol consumption and preference were analyzed via paired t-tests comparisons to baseline. Total fluid consumption was analyzed between baseline and Day 32 via paired t-tests. Significance was set at $p < 0.05$.

3. Results

3.1. Experiment I

Daily ethanol intake and preference during Experiment I are presented in Fig. 1. The baseline daily g/kg intake (average