



Research report

Sex differences in sensitivity to the social consequences of acute ethanol and social drinking during adolescence

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HIGHLIGHTS

- Social contributors to adolescent social drinking are sex-dependent.
- Pronounced ethanol-induced facilitation of play is seen in high drinking males.
- Pronounced social anxiety-like behavior is evident in high drinking females.
- High drinking females are sensitive to the socially anxiolytic effects of ethanol.

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ABSTRACT

In human adolescents, sociable males frequently drink to enhance positive emotional states, whereas anxious females often drink to avoid negative affective states. This study used a rat model of adolescence to provide information regarding possible sex differences in contributors to social drinking. The effects of ethanol (0, 0.5, and 0.75 g/kg) on play fighting and social preference were assessed on P30, P32, and P34 using a within-subject design. Then animals were tested in a social drinking paradigm (P37–P40), with this testing revealing high drinkers and low drinkers. Sex differences in sensitivity to ethanol emerged among high and low drinkers. High socially drinking males, but not females, when tested prior to drinking sessions, showed significant increases in play fighting at both doses. In low drinking males, play fighting was increased by 0.5 g/kg ethanol, whereas the higher dose of 0.75 g/kg produced significant decreases in play fighting. High drinking females initially showed low levels of social preference than high drinking males and low drinking females and were extremely sensitive to ethanol-induced enhancement of this social measure. Low social drinkers, both males and females, were more sensitive to the suppressing effects of ethanol on social preference following 0.75 g/kg ethanol. These findings indicate that during adolescence enhanced sensitivity to the facilitating effects of ethanol on play fighting is associated with heavy drinking among males, whereas low social preference together with high sensitivity to ethanol-induced enhancement of social preference is related to high social drinking in females.

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1. Introduction

Alcohol is one of the most widely used substances by American adolescents, with as many as 72.3% of 12th graders reporting lifetime alcohol use and 25.2% reporting binge drinking within the past 2 weeks [23]. A binge pattern of drinking that brings blood ethanol concentrations to ≥ 80 mg% and often corresponds to consuming 5 or more drinks for males, or 4 or more drinks for females,

is associated with an increased risk for alcohol abuse and dependence among adolescents (see [11]). A critical question regarding adolescent drinking is why do young people drink and sometimes drink excessively?

Young people drink predominantly in social situations, and the impact of social context on adolescent drinking is viewed as particularly important [39]. Analysis of drinking motives (i.e., reasons for drinking) revealed two distinct types of motives for adolescents who engage in heavy and problematic drinking [19,25]. Drinking to enhance positive emotional states is associated with high sociability, high impulsivity, and high levels of novelty and sensation seeking, with adolescent males reporting enhancement motives more frequently than adolescent females [10]. Drinking for coping reasons (i.e., drinking to avoid the experience of negative affective

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states) is associated with high levels of anxiety, especially anxiety in social situations, with adolescent females reporting coping reasons more frequently than their male counterparts [9]. These human data suggest that heavy drinkers among adolescent males may be more sensitive to socially facilitating effects of ethanol, whereas enhanced sensitivity to ethanol-associated anxiolysis may be characteristic of socially anxious adolescent females. Yet, it is difficult to disentangle from such studies whether reported drinking-related reductions in social anxiety reflect actual pharmacological properties of alcohol or are more a function of expectations of anxiolytic effects [3,46].

Much of the human research has also involved self-report questionnaires often given in a single session, which limits causal interpretation of the results. Whether enhanced sensitivity to socially facilitating effects of ethanol serves as a major contributor to heavy drinking in adolescent males, with accentuated sensitivity to anxiolytic effects of ethanol contributing to high intake in anxious adolescent females, has yet to be systematically investigated. These variables are difficult to examine in studies with human youth due to ethical considerations that preclude administration of alcohol to adolescents. Similarities found between human adolescents and adolescents of various mammalian species in terms of developmental history, behavioral changes, as well as neural and hormonal alterations provide reasonable justification for the use of animal models to study contributors to alcohol consumption during adolescence [43–45].

Using a simple animal model of adolescence and a modified social interaction test (see [59]), we have shown that adolescent rats, similar to their human counterparts, are sensitive to socially facilitating effects of ethanol. Relatively low doses of ethanol injected intraperitoneally (i.p.) enhance social behavior in adolescent rats tested in a familiar environment, with play fighting – an adolescent-typical form of social behavior – being predominantly activated. Ethanol-induced social facilitation declines during adolescence and is normally not evident by late adolescence or in adulthood [52–54,70]. Using a modification of the social interaction test that allows an experimental animal to freely move toward or away from a non-manipulated social partner in a two-compartment testing apparatus, social motivation can be estimated via calculation of a preference/avoidance coefficient during assessment of social behavior [59]. Through use of this modified social interaction test, we have found that under familiar, non-stressful and hence non-anxiety-provoking circumstances, adolescent animals demonstrate substantial social preference [52,55]. Further research has shown that social preference is especially sensitive to anxiogenic manipulations and anxiolytic compounds: significant decreases in social preference are evident following exposure to a stressor, with anxiolytic drugs being able to restore this decreased social preference to the levels demonstrated by non-stressed controls [15,33,55,57,58]. These findings suggest that diminished social preference in animals tested under familiar, non-anxiety-provoking circumstances can be viewed as an index of anxiety-like alterations in social interactions [15,57,58]. These anxiety-like behavioral alterations can be reversed or diminished by acute ethanol challenge [58], suggesting that animals with elevated levels of anxiety-like behavior, indexed via low levels of social preference, are sensitive to the socially anxiolytic effects of ethanol.

It has been shown that high levels of ethanol consumption are not restricted to human adolescents but are also evident in adolescents of other mammalian species, with for instance adolescent rats ingesting more ethanol relative to their body weights than do adults [14,20,40,67]. However the vast majority of animal models of ethanol intake have tested animals alone under circumstances where they are deprived of social stimuli, and many have also chronically housed the animals in social isolation (see [13] for a review). Assessment of drinking under social circumstances,

however, seems of considerable importance, given the prominent role of the social environment on ethanol intake, particularly during adolescence (see [1] for references and review).

Recent work in our laboratory using adolescent rats [63] demonstrated that responsiveness to a social peer predicts ethanol intake in a social setting – circumstances under which drinking typically occurs in human adolescents. High levels of social activity, including play fighting, in males and high levels of social anxiety-like behavior (indexed via low social preference) in females were associated with elevated social drinking. These data support the suggestion that males might be exceptionally sensitive to ethanol-induced social facilitation, ingesting ethanol for its socially enhancing properties, whereas females, especially those with enhanced social anxiety-like behavior, may be responsive to the socially anxiolytic effects of ethanol, ingesting it in order to diminish social anxiety-like behavior [63]. Given that an ethanol solution sweetened with sucrose and saccharin (“supersac”) was used in that study, the relationship between social responsiveness and “supersac” intake was subsequently assessed in a second experiment. In contrast to sweetened ethanol, there was no relationship between levels of social activity (that included play fighting) and “supersac” intake in either adolescent males or females, whereas levels of social anxiety-like behavior contributed to “supersac” intake in males, but not females. In contrast to high socially anxious females that demonstrated enhanced intake of sweetened ethanol, high socially anxious males demonstrated the lowest intake of “supersac”. These data clearly demonstrate notable differences in sex- and social behavior-dependent intake patterns between sweetened ethanol and the sweetened solution alone [63].

Therefore, the present study used a simple rat model of adolescence in combination with a novel model of social drinking to provide new information regarding possible sex differences in contributors to ethanol intake during adolescence, including sensitivity to the social consequences of acute ethanol. Specifically, this study was designed to test whether elevated ethanol intake in adolescent males is related to enhanced sensitivity to the socially facilitating effects of ethanol (indexed via ethanol-induced increases of play fighting), whereas high level of ethanol intake in females is associated with greater baseline levels of anxiety-like behavior (indexed via low levels of social preference) under social circumstances along with enhanced sensitivity to the socially anxiolytic effects of ethanol (indexed via ethanol-associated increases in social preference).

2. Methods

2.1. Subjects

Adolescent Sprague-Dawley male and female rats bred and reared in our colony at Binghamton University were used. A total of eight litters provided 40 male and female offspring to serve as experimental subjects and 40 to serve as partners. Animals were housed in a temperature-controlled (22 °C) vivarium, and maintained on a 12:12 h light:dark cycle (lights on at 0700 h) with ad libitum access to food (Purina rat chow) and water. Litters were culled to 10 pups (5 males and 5 females) within 24 h after birth on P0 and reared until weaning with their mothers in standard plastic maternity cages with pine shavings as bedding material. Rats were weaned on P21 and housed with their same-sex littermates. At all times, rats used in the current study were produced, maintained and treated in accordance with the guidelines for animal care established by the National Institutes of Health, using protocols approved by the Binghamton University Institutional Animal Care and Use Committee.

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