Available online at www.sciencedirect.com
SCIENCE DIRECT
Pharmacology, Biochemistry and Behavior 83 (2006) 307–313
PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR
www.elsevier.com/locate/pharmbiochembeh

# An inter-gender effect on ethanol drinking in rats: Proximal females increase ethanol drinking in males

Arthur Tomie *, Reka Hosszu [1], Rachel H. Rosenberg [1], Jennifer Gittleman [1], Patricia Patterson-Buckendahl [1], Larissa A. Pohorecky [1]

*Department of Psychology, Rutgers University, New Brunswick, NJ 08903, USA*
*Center of Alcohol Studies, Rutgers University, New Brunswick, NJ 08903, USA*

Received 14 July 2005; received in revised form 1 February 2006; accepted 11 February 2006
Available online 6 March 2006

**Abstract**

Three groups of male Long–Evans hooded rats were assessed for effects of social opportunity on drinking of ethanol or water. The ethanol/female group received intermittent presentations of a sipper containing ethanol that was followed by 15 s of social interaction opportunity with a female rat. The ethanol/male group received similar training except the social interaction opportunity was with a male rat. The water/female group received training similar to the ethanol/female group except that the sipper contained water. For the ethanol groups, the concentration of ethanol [3%, 4%, 6%, 8% and 10% (vol/vol)] in the sipper was increased across sessions. With 10% ethanol in the sipper, social opportunity with females induced more drinking and ethanol intake than did social opportunity with males. Social opportunity with females induced more intake of ethanol than water. Post-session plasma samples revealed social opportunity with females induced higher corticosterone and testosterone levels than did social opportunity with males, irrespective of the sipper fluid. This study documents, for the first time, an inter-gender effect on ethanol drinking in rats.


*Keywords:* Ethanol; Gender; Social Opportunity; Corticosterone; Testosterone; Rats

## 1. Introduction

There is considerable evidence that ethanol drinking is more likely in social situations in humans (Caudill and Lipscomb, 1980; Caudill and Marlatt, 1975) and, more recently, procedures have been developed that document social drinking effects in rats (Tomie et al., 2004a, 2004b, 2005). However, there are no published experimental reports evaluating in rats, inter-gender effects on ethanol drinking, even though in human beings there is considerable evidence supporting the premise that proximal females serve to increase ethanol drinking in males. For example, in studies of the effects of ethanol drinking in males, ethanol reduced anxiety induced by exposure to a female confederate (Lipscomb et al., 1980), increased ratings of sexual attractiveness of female confederates (Abbey et al., 2005), and enhanced expectations of social and physical pleasure after viewing females in a video (Corcoran and Segrist, 1993). Results of studies employing surveys and questionnaires also reveal that ethanol availability heightens sexual expectations (Morr and Mongeau, 2004), and males who self-report higher levels of ethanol drinking also report stronger expectations of increased social and physical pleasure as well as sexual enhancement (Mooney, 1995; Mooney et al., 1987).

The purpose of the present study was to evaluate experimentally inter-gender effects of proximal females on ethanol drinking in male rats. Experimental procedures were similar to those previously developed in our laboratory to study social drinking in male rats (Tomie et al., 2004a, 2004b, 2005). Briefly, male rats were provided with daily drinking sessions in an apparatus containing a retractable ethanol sipper tube and a guillotine door that separated the drinking chamber from a stainless steel wire mesh cage housing a conspecific male rat. Intermittent insertions of the ethanol sipper accompanied by

* Corresponding author. Department of Psychology, Rutgers University, New Brunswick, NJ 08903, USA. Tel.: +1 732 445 2423; fax: +1 732 445 2263.
*E-mail address:* tomie@rci.rutgers.edu (A. Tomie).
[1] Tel.: +1 732 445 2423; fax: +1 732 445 2263.

0091-3057/$ - see front matter © 2006 Elsevier Inc. All rights reserved.
doi:10.1016/j.pbb.2006.02.012

intermittent opportunities to socialize with the conspecific male rat in the wire mesh cage induced more ethanol drinking in the experimental male rat than water drinking in fluid controls (Tomie et al., 2004b) or ethanol drinking in controls not provided with social interaction opportunity (Tomie et al., 2004b, 2005). The present experiment utilizes these social drinking procedures to assess, for the first time, inter-gender effects on ethanol drinking by evaluating effects of social opportunity with female as compared to male rats, on ethanol drinking in male rats.

## 2. Methods

### 2.1. Animals and treatment

Adult male Long–Evans rats ($n=43$) and adult female Long–Evans hooded rats ($n=12$) were obtained from Harlan–Sprague–Dawley (Almont, NY, USA). Male rats were approximately 80 days old and weighed approximately 300 g at the beginning of the study. Female rats were approximately 65 days old and weighed approximately 180 g at the beginning of the study. Thirty-three male rats served as experimental subjects. Ten male rats and 12 female rats provided social opportunity during the drinking sessions. Procedures employing social opportunity with males were conducted from September through December 2003, while procedures employing social opportunity with females were conducted from May through August 2004, after the procedures employing social opportunity with males were completed. Experimental male rats ($n=12$) and 10 male rats that provided social opportunity from September through December 2003 were delivered to the laboratory at the end of August 2003. Experimental male rats ($n=21$) and 12 female rats that provided social opportunity from May through August 2004 were delivered to the laboratory at the end of April 2004. All rats were housed in individual suspended stainless steel cages and provided with free access to food and water throughout the study. Female rats were housed in a separate colony room with nine male rats, similar to those described above, that served as experimental rats for another study. In both colony rooms, there was a 12-h light, 12-h dark cycle (lights on at 0400 h). Estrous cycle was not assessed in the female rats in this study largely because of concerns regarding the effects of repeated daily vaginal lavage. Estrous cycle was unlikely a significant determinant of ethanol drinking, as variability in ethanol intake across sessions was at least as great in the ethanol/male group as in the ethanol/female group. All experimental procedures were performed in accordance with the guidelines of the Institutional Care and Use Committee of the National Institute of Drug Abuse, National Institutes of Health and the Guide for the Care and Use of Laboratory Animals (Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, 1996) and approved by the IACUC at Rutgers University.

### 2.2. Apparatus

Experimental chambers were those described in detail elsewhere (Tomie et al., 2004a, 2004b, 2005). Briefly, each chamber contained a graduated sipper tube mounted on a mechanical bottle insertion mechanism (BCS Machine, Plainfield, NJ, USA), which inserted the stainless steel sipper tube into the drinking chamber. The chamber also contained a guillotine door that separated the drinking chamber from a stainless steel wire mesh cage that housed either a conspecific male or female rat that provided social opportunity during the session. The guillotine door was operated by a pulley system connected to a mechanical door opening mechanism (BCS Machine, Plainfield, NJ, USA).

### 2.3. Drugs

Bulk ethanol (95%) was obtained from Rutgers University Chemical Stores. Ethanol was diluted in tap water to produce the concentrations (volume to volume, vol/vol) employed in the study.

### 2.4. Social opportunity procedures

Rats were run once daily 5–6 days/week and received 50 social opportunity trials per session for 42 daily training sessions. Prior to each session, rats were individually weighed and then immediately placed in the experimental drinking chambers. Rats that provided social opportunity during a session were placed in the wire mesh cage prior to the session. These rats were removed from the wire mesh cage between sessions and they were rotated across days among the seven chambers.

Rats were assigned to one of three groups. For all groups, the duration of the insertion of the sipper into the chamber was 10 s for each trial and the duration of access to social opportunity was 15 s for each trial. For rats in the ethanol/female group ($n=12$), the ethanol sipper was inserted into the drinking chamber immediately prior to the social opportunity, which consisted of the raising of the guillotine door separating the experimental male rat from the female rat in the wire mesh cage. The sipper was in the retracted position while the guillotine door was raised; therefore, when the stimulus rat was present, the experimental rat did not have access to the sipper. Rats in the ethanol/male group ($n=12$) received similar procedures, except the lifting of the guillotine door revealed a male rat in the wire mesh cage. Thus, the ethanol/female and ethanol/male groups both received the same procedures, differing only with respect to the gender of the social opportunity (female vs. male). Rats in the water/female group ($n=9$) received training similar to the ethanol/female group except that throughout the experiment the fluid in the sipper was water rather than ethanol. The sequence of training procedures for the three groups is presented in Table 1. Training was conducted with each ethanol concentration until mean session-to-session variability in grams per kilogram ethanol intake did not vary by more than 10% between two consecutive sessions.

For all groups, the mean inter-trial interval (ITI) was 60 s (±15 s) and the session duration was approximately 50 min. Volume of fluid consumed (ml) was determined by recording the fluid level in the tube immediately before and after each drinking session. Extensive but unsystematic observations

Table 1
Mean milliliters drinking

| Treatment | Sessions | Groups | | |
|---|---|---|---|---|
| % Ethanol concentrations | | Ethanol/ male | Ethanol/ female | Water/ female |
| 3 | 1–10 | 1.8±0.3 | 1.3±0.4 | 0.6±0.2 |
| 4 | 11–20 | 2.2±0.4 | 2.7±0.6 | 0.8±0.4** |
| 6 | 21–26 | 3.9±0.6 | 4.3±0.9 | 0.8±0.1** |
| 8 | 27–32 | 3.3±0.4 | 3.7±0.6 | 0.7±0.2** |
| 10 | 33–42 | 3.6±0.5** | 5.6±0.4 | 1.1±0.2** |

Water/female group received water in the sipper during all sessions (1–42). Mean milliliters drinking presented as a function of ethanol concentrations (3% to 10%) are based on the last 2 days of training with each concentration. Double asterisk (**) indicates that the ethanol/female group differed significantly from the ethanol/male group (Fisher's LSD, $P<0.01$) or that the ethanol/female group differed significantly from the water/female group (Fisher's LSD, $P<0.01$).

revealed that raising of the guillotine door was typically followed by social interactions between the experimental rat and the conspecific rat housed in the wire mesh cage. Behaviors commonly observed in experimental rats were rearing, sniffing, nose poking and pawing, which were directed at the wire mesh surface of the holding cage that separated the drinking chamber from the conspecific rat in the holding cage.

### 2.5. Plasma ethanol, corticosterone and testosterone assays

Immediately after the last drinking session on day 42, approximately 50 μl of tail blood was collected in heparinized tubes from a tail snip. All blood samples were collected within 2 min of cutting the tail. Samples were centrifuged and frozen at −70 °C until analyzed. Duplicate plasma samples were assayed for blood ethanol levels by using ethyl alcohol test kit (Product #229-29, Diagnostic Chemicals, Ltd., Oxford, CT, USA) and for testosterone levels using radioimmunoassay (125I RIA Kit, Product #07-189102, MP Biomedicals, Irvine, CA, USA). Plasma corticosterone was assayed by radioimmunoassay (3H RIA kit, Product #07-120002, MP Biomedicals, Irvine, CA, USA) using a tritium label for corticosterone and a highly specific corticosterone antiserum with a detection threshold of 0.1 μg/100ml. Corticosterone and testosterone samples did not vary by more than 10% between duplicate pairs.

### 2.6. Analyses

For each subject in each drinking session, volume of fluid consumed (ml) and body weight (kg) were measured, then grams of fluid consumed per kilogram of body weight (g/kg fluid intake) and grams of ethanol consumed per kilogram of body weight (g/kg ethanol intake) were derived. Group differences in drinking as a function of social opportunity gender (female vs. male) and fluid (ethanol vs. water) and ethanol concentrations [3%, 4%, 6%, 8% and 10% (vol/vol)] were conducted on the mean of the last two sessions of training with each concentration. Effects of ethanol concentrations on mean daily milliliters drinking and mean daily grams per kilogram ethanol intake for the ethanol/female and the ethanol/male groups were assessed by mixed-design two-way repeated-measures multivariate analysis of variance using MANOVA (Systat Statistical Software, Richmond, CA, USA). A similar analysis assessed effects of ethanol concentrations on mean daily milliliters drinking and mean daily grams per kilogram fluid intake for the ethanol/female and the water/female groups. Fisher's least significant difference (LSD) test provided pair-wise comparisons at individual points ($P<0.01$). Group mean plasma corticosterone levels are presented as mean nanograms per milliliter (±standard error) and as mean nanomoles per liter (±standard error). The conversion factor used was: nmol/l=(ng/ml)*(2.89). Group mean blood ethanol levels are presented as mean milligrams per deciliter (±standard error) and as mean millimoles per liter (±standard error). The conversion factor used was: mmol/l=(mg/dl)/(4.60). Group mean plasma testosterone levels are presented as mean nanograms per milliliter (±standard error) and as mean millimoles per liter (±standard error). The conversion factor used was: mmol/l=(ng/ml)*(3.47). Group differences in mean plasma corticosterone levels and group mean blood ethanol levels and group mean plasma testosterone levels were each evaluated by one-way analysis of variance using ANOVA (Systat Statistical Software, Richmond, CA, USA) followed by Student's–Newman–Keuls post hoc analysis ($P<0.05$). For the 24 rats with ethanol in the sipper, the correlation between an individual rat's grams per kilogram ethanol intake on day 42 and that rat's plasma ethanol level in samples taken immediately following the training session on day 42 was determined using Pearson's product-moment correlation coefficient (Regression Analysis, Systat Statistical Software, Richmond, CA, USA).

## 3. Results

### 3.1. Initiation of drinking from the sipper

During sessions 1–10, all 24 rats in the ethanol/male and ethanol/female groups initiated drinking of the 3% ethanol solution in the sipper CS. Mean daily drinking during sessions 7–10 were greater than 1.0 ml for both groups. All nine rats in the water/female group initiated drinking of water from the sipper CS, though mean daily drinking during sessions 7–10 were never greater than 0.7 ml.

### 3.2. Intake of higher concentrations of ethanol

Mean daily milliliters drinking on the last two sessions when the sipper contained 3%, 4%, 6%, 8% and 10% ethanol for each of the three groups are presented in Table 1. For the ethanol/female and ethanol/male groups, analysis revealed no significant main effect of social opportunity gender [$F(1,22)<1$], a significant main effect of concentrations [$F(4,88)=38.251$, $P<0.01$] and a significant interaction effect between social opportunity gender and concentrations [$F(4,88)=2.943$, $P<0.05$]. Fisher's LSD revealed significantly higher milliliter fluid drinking ($P<0.05$) in the ethanol/female group than in the ethanol/male group when the concentration of ethanol in the sipper was 10% (vol/vol). A similar analysis of mean daily grams per kilogram ethanol intake (see Fig. 1, top panel)

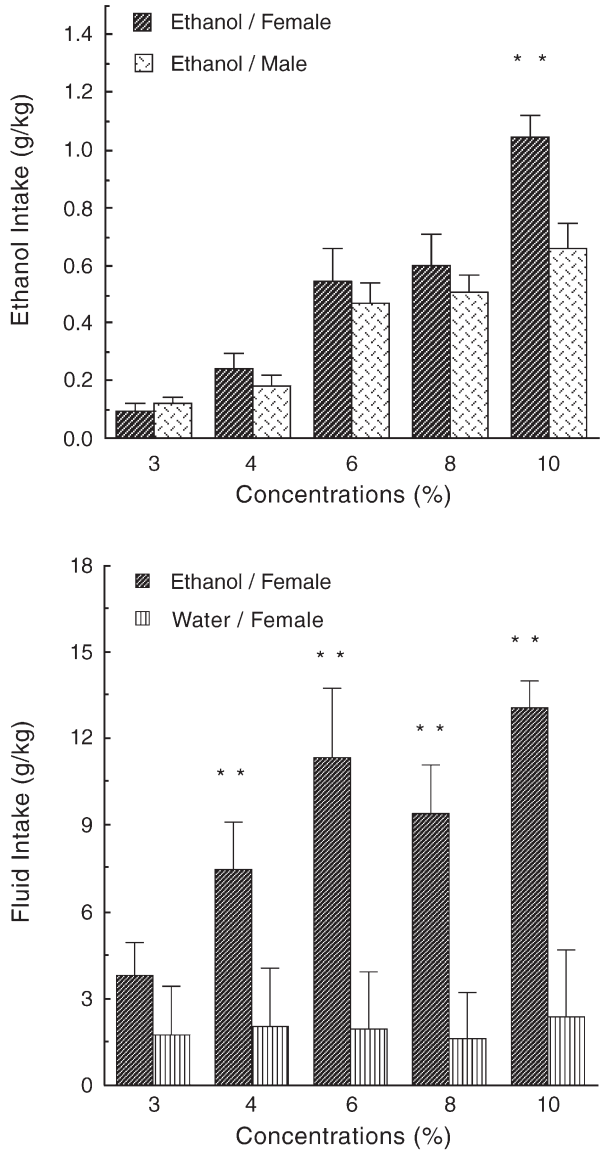


Fig. 1. Top panel: mean grams of ethanol consumed per kilogram of body weight (g/kg) on the last two sessions of training when the sipper contained 3%, 4%, 6%, 8% and 10% ethanol (vol/vol). Rats in the ethanol/female group and the ethanol/male group experienced the same social opportunity procedures, differing only in the gender (female vs. male) of the social opportunity. Vertical bars represent the standard error of the mean (S.E.M.). Double asterisk (**) indicates that the groups differed significantly (Fisher's LSD, $P<0.01$). Bottom panel: mean grams of fluid consumed per kilogram of body weight (g/kg) on the last two sessions of training when the sipper for the ethanol/female group contained 3%, 4%, 6%, 8% and 10% ethanol (vol/vol). Sipper for the water/female group contained water throughout the study. Vertical bars represent the standard error of the mean (S.E.M.). Double asterisk (**) indicates that the groups differed significantly (Fisher's LSD, $P<0.01$).

revealed no significant main effect of social opportunity gender [$F(1,22)=2.176$, $P>0.10$], a significant main effect of concentrations [$F(4,88)=66.782$, $P<0.01$] and a significant interaction effect between social opportunity gender and concentrations [$F(4,88)=4.663$, $P<0.01$]. Fisher's LSD revealed significantly higher mean grams per kilogram ethanol intake ($P<0.01$) in the ethanol/female group than in the ethanol/male group when the concentration of ethanol in the sipper was 10% (vol/vol). Thus, the opportunity to interact with female rats induced significantly higher mean daily ethanol intake of the highest concentration of ethanol [10% (vol/vol)].

Social opportunity with females induced more drinking of ethanol fluid than water. Analysis of mean daily milliliters drinking (see Table 1) for the ethanol/female and water/female groups during the last 2 days when the ethanol/female group received training with each of the ascending concentrations of ethanol revealed a significant main effect of fluid [$F(1,19)=22.120$, $P<0.01$], a significant main effect of concentrations [$F(4,76)=13.429$, $P<0.01$] and a significant interaction effect between fluid and concentrations [$F(4,76)=9.372$, $P<0.01$]. Fisher's LSD revealed significantly higher milliliter fluid drinking ($P<0.01$) in the ethanol/female group than in the water/female group when the concentration of ethanol in the sipper for the ethanol/female group was 4%, 6%, 8% and 10% (vol/vol). A similar analysis of mean daily grams per kilogram fluid intake (see Fig. 1, bottom panel) revealed a significant main effect of fluid [$F(1,19)=18.665$, $P<0.01$], a significant main effect of concentrations [$F(4,76)=8.811$, $P<0.01$] and a significant interaction between fluid and concentrations [$F(4,76)=7.220$, $P<0.01$]. Fisher's LSD revealed significantly higher gram per kilogram fluid intake ($P<0.01$) in the ethanol/female group than in the water/female group when the concentration of ethanol in the sipper for the ethanol/female group was 4%, 6%, 8% and 10% (vol/vol). Thus, when provided with the opportunity to interact with female rats, male rats provided with ethanol in the sipper CS drank significantly more milliliters of fluid than did male rats provided with water in the sipper CS. This difference was also observed in the weight-adjusted measure of intake, indicating that the effect is not due to group differences in body weight.

### 3.3. Plasma ethanol, corticosterone and testosterone levels

Mean plasma ethanol levels for the ethanol/female and ethanol/male groups are presented in Table 2. Analysis revealed that these groups differed significantly [$F(1,22)=14.565$, $P<0.01$]. This is consistent with the higher levels of ethanol intake in the ethanol/female group and suggests that reductions

Table 2
Plasma levels of ethanol, corticosterone and testosterone

| Plasma levels | Groups | | |
|---|---|---|---|
| | Ethanol/male | Ethanol/female | Water/female |
| Ethanol (mg/dl) | 29±7** | 101±17 | NA |
| Ethanol (mmol/l) | 6.4±1.7** | 22.1±3.7 | NA |
| Corticosterone (ng/ml) | 98±15.6* | 319±37.6 | 333±40.4 |
| Corticosterone (nmol/l) | 283±45* | 922±109 | 962±117 |
| Testosterone (ng/ml) | 0.78±0.14* | 2.39±.54 | 3.26±0.62 |
| Testosterone (nmol/l) | 2.7±0.5* | 8.3±1.9 | 11.3±2.2 |

NA indicates that plasma ethanol levels were not assessed in the water/female group. Single asterisk (*) and double asterisk (**) indicate that the ethanol/female group differed significantly from the ethanol/male group (Fisher's LSD, $P<0.05$ and $P<0.01$, respectively).

in the volume of ethanol fluid in the sipper tubes during the session were due to drinking rather than spillage. For the 24 rats with ethanol in the sipper, there was a significant positive correlation between an individual rat's grams per kilogram ethanol intake on day 42 and that rat's plasma ethanol level in samples taken immediately following the training session on day 42 [Pearson's $r=+0.817$, $P<0.01$].

Mean plasma corticosterone levels for the three groups are presented in Table 2. Analysis revealed a significant effect of groups [$F(2,29)=18.456$, $P<0.01$]. Student's–Newman–Keuls post hoc analysis revealed that the ethanol/female group had significantly higher plasma corticosterone levels than the ethanol/male group ($P<0.05$) and the water/female group had significantly higher plasma corticosterone levels than the ethanol/male group ($P<0.05$). Thus, each of the groups with female social opportunity had higher mean plasma corticosterone levels than did the group with male social opportunity.

Mean plasma testosterone levels for the three groups are presented in Table 2. Analysis revealed a significant effect of groups [$F(2,25)=6.426$, $P<0.01$]. Student's–Newman–Keuls post hoc analysis revealed that the ethanol/female group had significantly higher plasma testosterone levels than the ethanol/male group ($P<0.05$) and the water/female group had significantly higher plasma testosterone levels than the ethanol/male group ($P<0.05$). Thus, each of the groups with female social opportunity had higher mean plasma testosterone levels than did the group with male social opportunity.

## 4. Discussion

### 4.1. Intake of increasing concentrations of ethanol

During training with the highest concentration of ethanol in the sipper [10% (vol/vol)], the ethanol/female group showed significantly more milliliters drinking and significantly more grams per kilogram ethanol intake than the ethanol/male group. Social opportunity with females induced over 50% more milliliters drinking and over 50% more grams per kilogram ethanol intake than did social opportunity with males. In the two groups receiving social opportunity with females, across the four blocks of ethanol concentrations, ethanol in the sipper induced more milliliters drinking and grams per kilogram fluid intake than water in the sipper, and the groups differed significantly when the sipper for the ethanol/female group contained 4%, 6%, 8% and 10% ethanol. As ethanol concentrations increased for the ethanol/female group, mean milliliters water drinking for the water/female group did not change appreciably. In contrast, mean milliliters drinking of the ethanol fluid for the ethanol/female group increased approximately four-fold, suggesting that fluid intake escalated for the ethanol/female group more so than for the water/female group.

Inter-gender effects on ethanol drinking and ethanol intake in rats are reported here for the first time. We are aware of no previously published experimental reports that compare the effects of proximal females vs. proximal males on ethanol drinking or ethanol intake in rats. While numerous ethanol drinking studies have evaluated gender effects in rats, they compared contemporaneous ethanol drinking in females vs. males, and do not vary the presence of one gender to evaluate their effects on the ethanol drinking of the other.

While acknowledging the difficulties of interspecies comparisons, it should be noted, nevertheless, that reports of inter-gender effects on ethanol drinking in human beings are also scarce. For example, in human beings, there are no published reports documenting the effects of proximal females on amount of ethanol drinking in males. Studies of modeling of ethanol drinking differ from the present study in that they assess effects of ethanol drinking of the confederate on ethanol drinking by the participant. These modeling studies have employed confederates of the same gender (Caudill and Kong, 2001; Caudill and Lipscomb, 1980; Caudill and Marlatt, 1975) or have reported that male participants modeled more closely the choice of alcoholic beverages of male confederates than female confederates (Corcoran, 1995). There are, however, factors that may encourage males to drink more ethanol in the presence of proximal females. For example, ethanol drinking has been reported to increase expectations of sexual pleasure (Abrahamson, 2004; Friedman et al., 2005; Johnson and Stahl, 2004; Mooney, 1995; Morr and Mongeau, 2004; Wilson, 1981) and to reduce anxiety levels related to sexual situations (De Boer et al., 1993; Dolan and Nathan, 2002; Keane and Lisman, 1980; Lipscomb et al., 1980). Thus, there are reasons to expect that proximal females will induce ethanol drinking in males; nevertheless, reports of inter-gender effects on ethanol drinking in human beings or in rats are absent from the literature.

### 4.2. Plasma corticosterone

Social opportunity with females induced higher mean plasma corticosterone levels in males than did social opportunity with males. This effect on plasma corticosterone is consistent with previous reports showing that the presence of female rats induced elevated corticosterone levels in male rats (Retana-Marquez et al., 2003; Taylor et al., 1987), and the present data extend this finding to ethanol drinking situations, as well. The higher levels of drinking of 10% ethanol in the ethanol/female group than the ethanol/male group may be mediated by the higher levels of corticosterone induced by proximal females, as there is abundant evidence that corticosterone induces ethanol intake. For example, in rats, elevations in corticosterone levels and increased ethanol drinking are induced by electric shock (Hatton and Veith, 1974; Opsahl and Hatton, 1972), food deprivation (Hansen et al., 1995; Prasad and Prasad, 1995) and social stress (Blanchard et al., 1993; Nunez et al., 2002), while adrenalectomy (Fahlke et al., 1994a) or injections of the corticosterone inhibitor metyrapone (Fahlke et al., 1994b) reduced corticosterone levels and decreased ethanol intake in rats. Furthermore, ethanol intake levels were restored by corticosterone replacement therapy (Fahlke and Eriksson, 2000; Fahlke et al., 1996). Thus, the inter-gender effect on ethanol drinking may be due to the effects of proximal females on corticosterone release. While there is some evidence that ethanol increases corticosterone levels (Seeley et al., 1996; Valdez et al., 2004), it is unlikely that the effects of gender on corticosterone levels were

mediated by ethanol drinking, because even with water in the sipper, social opportunity with females induced higher post-session levels of corticosterone than did social opportunity with males accompanied by ethanol in the sipper.

### 4.3. Plasma testosterone

Social opportunity with female rats induced significantly higher plasma testosterone levels than did social opportunity with male rats, regardless of the presence of ethanol in the sipper. This is consistent with numerous studies documenting the testosterone elevating effects of females in rats (Amstislavskaya and Popova, 2004; Flannelly and Lore, 1977; Graham and Desjardins, 1980; Kamel et al., 1975; Taylor et al., 1987), in mice (Amstislavskaya and Popova, 2004; Kavaliers et al., 2001; Macrides et al., 1975) and in human beings (Roney et al., 2003). It is unlikely that the differences in plasma testosterone levels observed in the present study are due to inter-gender effects on ethanol intake, as exposure to ethanol decreases testosterone levels in rats (Apter and Eriksson, 2003; Blanchard et al., 1993; Yudko, 1998). With water in the sipper, social opportunity with females induced higher post-session levels of testosterone than when social opportunity with males was accompanied by ethanol in the sipper, suggesting that the effects of gender on testosterone levels are not due to ethanol's effects on testosterone. Finally, it should be noted that ethanol injections increase sexual motivation of male rats for receptive female rats (Ferraro and Kiefer, 2004); therefore, in the present study, this effect of ethanol may have increased the reward value of socializing with females.

### 4.4. Conclusions

Inter-gender effects on ethanol drinking in rats are reported here for the first time. Social opportunity with female rats induced more intake of 10% ethanol in male rats than did social opportunity with male rats. In the groups provided with social opportunity with female rats, ethanol fluid intake was at least four times greater than water fluid intake and this effect was evident across all of the higher ethanol concentrations (6%, 8% and 10%). Note, however, that ethanol fluid intake in the ethanol/male group was also much higher than water fluid intake in the water/female group, indicating that ethanol in the sipper CS induces more drinking than the water in the sipper CS, regardless of the gender of the social opportunity. In a previous study providing for social opportunity with male rats (Tomie et al., 2004b), ethanol fluid intake from the sipper CS was much higher than water fluid intake from the sipper CS, indicating that the fluid effect observed in the present study was not specific to the gender of the social opportunity. With ethanol in the sipper, social opportunity with females, as compared to with males, induced higher post-session levels of corticosterone and testosterone. With water in the sipper, social opportunity with females induced higher post-session levels of corticosterone and testosterone than when social opportunity with males was accompanied by ethanol in the sipper, suggesting that the effects of gender on corticosterone or testosterone levels were not due to ethanol's effects on these hormones. The results suggest that these social drinking procedures provide conditions conducive to the study of inter-gender effects on ethanol drinking in rats.

## Acknowledgment

This research was supported in part by NIAAA grant R21 AAA-12023 awarded to A.T., by NIAAA grant R21 AAA-14399-01A2 awarded to P.B-P P, and by funds from the Center of Alcohol Studies, Rutgers University awarded to L.A.P.

## References

Abbey A, Zawacki T, Buck PO. The effects of past sexual assault perpetration and alcohol consumption on men's reactions to women's mixed signals. J Soc Clin Psychol 2005;24:129–55.

Abrahamson M. Alcohol in courtship contexts: focus-group interviews with young Swedish women and men. Contemp Drug Probl 2004;31:3–29.

Amstislavskaya TG, Popova NK. Female-induced sexual arousal in male mice and rats: behavioral and testosterone response. Horm Behav 2004;46:544–50.

Apter SJ, Eriksson CJP. The effect of alcohol on testosterone concentrations in alcohol preferring and non-alcohol preferring rat lines. Alcohol Clin Exp Res 2003;27:1190–3.

Blanchard RJ, Yudko EB, Blanchard DC. Alcohol, aggression and the stress of subordination. J Stud Alcohol 1993;Suppl 11:146–55.

Caudill BD, Kong FH. Social approval and facilitation in predicting modeling effects in alcohol consumption. J Subst Abuse 2001;13:425–41.

Caudill BD, Lipscomb TR. Modeling influences on alcoholics rates of alcohol consumption. J Appl Behav Anal 1980;13:355–65.

Caudill BD, Marlatt GA. Modeling influences in social drinking: an experimental analogue. J Consult Clin Psychol 1975;43:405–15.

Corcoran KJ. Cognitive and situational factors predict alcoholic beverage selection. Addict Behav 1995;20:525–42.

Corcoran KJ, Segrist DJ. Personal expectancies and group influences affect alcoholic beverage selection: the interaction of personal and situational variables. Addict Behav 1993;18:577–82.

De Boer MC, Schippers GM, Van der Staak CP. Alcohol and social anxiety in women and men: pharmacological and expectancy effects. Addict Behav 1993;18:117–26.

Dolan SL, Nathan PE. When one marital partner is an alcoholic. In: Harvey JH, Wenzel A, editors. A clinician's guide to maintaining and enhancing close relationships. Mahwah, NJ: Lawrence Erlbaum Associates; 2002. p. 215–29.

Fahlke C, Eriksson CJP. Effect of adrenalectomy and exposure to corticosterone on alcohol intake in alcohol-preferring and alcohol-avoiding rat lines. Alcohol Alcohol 2000;35:139–44.

Fahlke C, Engel JA, Eriksson CJP, Hard E, Soderpalm B. Involvement of corticosterone in the modulation of ethanol consumption in the rat. Alcohol 1994a;11:195–202.

Fahlke C, Hard E, Thomasson R, Engel JA, Hansen S. Metyrapone-induced suppression of corticosterone synthesis reduced ethanol consumption in high-preferring rats. Pharmacol Biochem Behav 1994b;48:977–81.

Fahlke C, Hard E, Hansen S. Facilitation of ethanol consumption by intracerebroventricular infusions of corticosterone. Psychopharmacology 1996;127:133–9.

Ferraro III FM, Kiefer SW. Behavioral analysis of male rat sexual motivation and performance following acute ethanol treatment. Pharmacol Biochem Behav 2004;78:427–33.

Flannelly KJ, Lore R. The influence of females upon aggression in domesticated male rats (*Rattus norvegicus*). Animal Behav 1977;25:654–9.

Friedman RS, McCarthy DM, Forester JS, Denzler M. Automatic effects of alcohol cues on sexual attraction. Addict 2005;100:672–81.

Graham JM, Desjardins C. Classical conditioning: induction of luteinizing hormone and testosterone secretion in anticipation of sexual activity. Science 1980;210:1039–41.

Hansen S, Fahlke C, Soderpalm AHV, Hard E. Significance of adrenal corticosteroid secretion for the food restriction-induced enhancement of alcohol drinking in the rat. Psychopharmacology 1995;121:213–21.

Hatton GI, Veith A. Stress-related and diurnal alcohol drinking in rats. Psychon Sci 1974;4:195–6.

Institute of Laboratory Animal Resources Commission on Life Sciences, National Research Council, 1996.

Johnson TJ, Stahl C. Sexual experiences associated with participation in drinking games. J Gen Psychol 2004;131:304–20.

Kamel F, Mock EJ, Wright WW, Frankel AI. Alterations in plasma concentrations of testosterone, LH, and prolactin associated with mating in the male rat. Horm Behav 1975;6:277–88.

Kavaliers M, Choleris E, Colwell DD. Brief exposure to female odors emboldens male mice by reducing predator-induced behavioral and hormonal responses. Horm Behav 2001;40:497–509.

Keane TM, Lisman SA. Alcohol and social anxiety in males: behavioral, cognitive, and physiological effects. J Abnormal Psychol 1980;89:213–23.

Lipscomb TR, Nathan PE, Wilson GT, Abrams DB. Effects of tolerance on the anxiety-reducing function of alcohol. Arch Gen Psychiatry 1980;37: 577–82.

Macrides F, Bartke A, Dalterio S. Strange female increases plasma testosterone levels in male mice. Science 1975;189:1104–6.

Mooney DK. The relationship between sexual insecurity, the alcohol expectation for enhanced sexual experience, and consumption patterns. Addict Behav 1995;20:243–50.

Mooney DK, Fromme K, Kivlahan DR, Marlatt GA. Correlates of alcohol consumption: sex, age, and expectancies relate differentially to quantity and frequency. Addict Behav 1987;12:235–40.

Morr MC, Mongeau PA. First-date expectations: the impact of sex of initiator, alcohol consumption, and relationship type. Commun Res 2004;31:3–35.

Nunez MJ, Rivas M, Riveiro P, Suarez J, Balboa J, Nunez LA, et al. Effects of nefazodone on voluntary ethanol consumption induced by isolation stress in young and aged rats. Pharmacol Biochem Behav 2002;73:689–96.

Opsahl CA, Hatton GI. Volitional ethanol increases during acquisition and extinction of avoidance responding. Physiol Behav 1972;8:87–93.

Prasad C, Prasad A. A relationship between increased voluntary alcohol preference and basal hypercorticosteronemia associated with an attenuated rise in corticosterone output during stress. Alcohol 1995;12:59–63.

Retana-Marquez S, Bonilla-Jaime H, Vazquez-Palacios G, Martinez-Garcia R, Velazquez-Montezuma J. Changes in masculine sexual behavior, corticosterone and testosterone in response to acute and chronic stress in male rats. Horm Behav 2003;44:327–37.

Roney JR, Mahler SV, Maestripieri D. Behavioral and hormonal responses of men to brief interactions with women. Evol Human Behav 2003;24:365–75.

Seeley RJ, Hawkins MH, Ramsay DS, Wilkinson CW. Learned tolerance to the corticosterone-increasing action of ethanol in rats. Pharmacol Biochem Behav 1996;55:269–73.

Taylor GT, Weiss J, Rupich R. Male rat behavior, endocrinology and reproductive physiology in a mixed-sex, socially stressful colony. Physiol Behav 1987;39:429–33.

Tomie A, Burger KM, Di Poce J, Pohorecky LA. Social opportunity and ethanol drinking in rats. Prog Neuro-Psychopharmacol Biol Psychiatry 2004a;28: 1089–97.

Tomie A, Uveges JM, Burger KM, Patterson-Buckendahl P, Pohorecky LA. Effects of ethanol sipper and social opportunity on ethanol drinking in rats. Alcohol Alcohol 2004b;39:197–202.

Tomie A, Gittleman J, Dranoff E, Pohorecky LA. Social interaction opportunity and intermittent presentations of ethanol sipper tube induce ethanol drinking in rats. Alcohol 2005;35:43–55.

Valdez GR, Sabino V, Koob GF. Increased anxiety-like behavior and ethanol self-administration in dependant rats: reversal via corticotropin-releasing factor-2 receptor activation. Alcohol Clin Exp Res 2004;28:865–72.

Wilson GT. The effects of alcohol on human sexual behavior. Adv Subst Abuse 1981;2:1–40.

Yudko EB. Individual differences in subordinates housed in the visible burrow system. Dis Abst Int: Sec B: Sci Eng 1998;58(11-B).