Available online at www.sciencedirect.com
ScienceDirect
Pharmacology, Biochemistry and Behavior 87 (2007) 341 – 348
PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR
www.elsevier.com/locate/pharmbiochembeh

# Intermittent exposure to a social stimulus enhances ethanol drinking in rats

Arthur Tomie *, Kandia Lewis, Jodi Curiotto, Larissa A. Pohorecky

*Department of Psychology, 152 Freylinghuysen Road, Rutgers University, Piscataway, NJ 08854-8020, United States*

Received 7 December 2006; received in revised form 10 May 2007; accepted 11 May 2007
Available online 21 May 2007

**Abstract**

The present experiment evaluates the effects of intermittent exposure to a social stimulus on ethanol and water drinking in rats. Four groups of rats were arranged in a 2×2 factorial design with 2 levels of Social procedure (Intermittent Social vs Continuous Social) and 2 levels of sipper Liquid (Ethanol vs Water). Intermittent Social groups received 35 trials per session. Each trial consisted of the insertion of the sipper tube for 10 s followed by lifting of the guillotine door for 15 s. The guillotine door separated the experimental rat from the conspecific rat in the wire mesh cage during the 60 s inter-trial interval. The Continuous Social groups received similar procedures except that the guillotine door was raised during the entire duration of the session. For the Ethanol groups, the concentrations of ethanol in the sipper [3, 4, 6, 8, 10, 12, 14, and 16% (vol/vol)] increased across sessions, while the Water groups received 0% ethanol (water) in the sipper throughout the experiment. Both Social procedures induced more intake of ethanol than water. The Intermittent Social procedure induced more ethanol intake at the two highest ethanol concentration blocks (10–12% and 14–16%) than the Continuous Social procedure, but this effect was not observed with water. Effects of social stimulation on ethanol drinking are discussed.


*Keywords:* Intermittent; Social; Ethanol; Schedule-induced polydipsia; Autoshaping; Rats

## 1. Introduction

In human beings, ethanol drinking is associated with socializing. Investigators have reported that human beings drink more ethanol in social interaction situations compared to control subjects in similar environments that are not permitted to engage in social interactions (Abrams & Niaura, 1987; Caudil & Kong, 2001; Maisto et al., 1999). The positive relationship between social stimulation and ethanol drinking has recently been reported in animals as well. In these studies groups of male rats receiving intermittent presentations of a social stimulus (conspecific male rat) exhibited higher levels of ethanol intake than did controls that did not receive the social stimulus (Tomie et al., 2004b, 2005). While the group that had social stimulation drank more ethanol than the group that did not, these studies did not include control groups that received the social stimulus continuously, leaving unclear whether the effects on ethanol drinking were due to the duration of exposure to the social stimulus or to the intermittent scheduling of the social stimulus presentations.

There is evidence, in studies of water drinking, that continuous social stimulation reduced water drinking relative to groups receiving intermittent presentations of a social stimulus (Hudson and Singer, 1979). In their studies, more water drinking was induced in monkeys (*Macaca fascicularis*), receiving intermittent exposures to a social stimulus consisting either of a visual display of a primate (Hudson and Singer, 1979) Exp 1, or the viewing of another nearby monkey (Hudson and Singer, 1979) Exp 2, than in controls receiving continuous exposure to these social stimuli. This suggests that in monkeys water drinking was induced by the intermittent scheduling of the social stimulus, rather than the duration of exposure to the social stimulus.

The present study assessed in rats the effects on ethanol drinking of the duration of social stimulation by providing for either intermittent social stimulation or for continuous social stimulation during the entire duration of the daily ethanol drinking session. In addition, the present study also assessed, in liquid control groups, the effects of the duration of social stimulation on water drinking as well. While previous studies have reported that social stimulation induces more ethanol

* Corresponding author. Tel.: +1 732 445 2423; fax: +1 732 445 2263.
*E-mail address:* tomie@rci.rutgers.edu (A. Tomie).

0091-3057/$ - see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1016/j.pbb.2007.05.008

drinking than water drinking in rats (Tomie et al., 2004b), the effects of the duration of social stimulation on water drinking in rats were not evaluated. Thus, the present experiment assessed the effects of the duration of social stimulation (Intermittent Social Stimulus procedure vs Continuous Social Stimulus procedure) on ethanol and water drinking in rats.

## 2. Methods

### 2.1. Animals

Forty adult male Long–Evans hooded rats served as experimental subjects and 11 adult male Long–Evans hooded rats served as the social stimulus during the drinking sessions. All 51 rats were obtained from Harlan-Sprague–Dawley, Almont, NY, USA and weighed between 240 g and 266 g at the beginning of the study. All rats were individually housed in suspended stainless steel cages with free access to food and water, in a colony room with a 12-h light, 12-h dark cycle (lights on at 0400 h). All experimental procedures were performed in accordance with the guidelines of the Institutional Care and Use Committee of the National Institute on 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. Drugs

Ethanol solutions were made volume to volume (vol/vol) by diluting 95% ethyl alcohol (Rutgers University, Chemical Stores, New Brunswick, NJ, USA) with tap water.

### 2.3. Apparatus

Experimental chambers were 7 locally constructed cubicles (24 cm × 24 cm × 26 cm; $L \times W \times H$) with a floor consisting of stainless steel rods. The right wall of each chamber was an intelligence panel equipped with a retractable stainless steel sipper tube and a stainless steel guillotine door. The sipper tube contained a stainless steel ball-bearing with an inserted rubber stopper used for holding the liquid in a 50 ml Plexiglas graduated tube (Model 58320, Kimble-Kontes, Vineland, NJ, USA). The graduated tube was mounted on a mechanical bottle insertion mechanism (BCS Machine, Plainfield, NJ, USA), which inserted the stainless steel sipper tube through an aperture located 4 cm above the floor and 6 cm to the left of the front wall. The sipper insertion mechanism moved the sipper tube a total of 2.75 cm from the fully retracted to the fully inserted positions. In the fully inserted position, the tip of the sipper tube was 0.5 cm into the chamber. The guillotine door (11 cm × 13 cm; $H \times W$) separated the chamber from a stainless steel wire mesh cage (20 cm × 10 cm × 12 cm; $L \times W \times H$) that during the procedures housed a conspecific male of approximately the same age and weight as the experimental subject. The left edge of the guillotine door was located 0.5 cm to the right of the back wall. The guillotine door was operated by a pulley system connected to a mechanical door opening mechanism (BCS Machine, Plainfield, NJ, USA). Each chamber was powered by a 28 V DC power supply, and session events were controlled by IBM-compatible PCs equipped with I/O relay cards (Model PCL-725, JDR Microdevices, San Jose, CA, USA).

### 2.4. Procedures

Rats were run 5–6 days a week in daily sessions conducted between 0900 and 1600 h. Before each session, the rats were individually weighed and then immediately placed in the experimental chambers. Male Long–Evans hooded rats ($n = 11$) of approximately the same age as the experimental subjects did not undergo experimental procedures, but served as the social stimulus during the session. These rats were housed in the same colony room as described earlier for experimental subjects. These rats were placed in the wire mesh cage before the session and were removed from the cage between sessions. In addition, these rats were rotated across days between the seven chambers.

The 40 rats that served as experimental subjects were randomly assigned to one of 4 groups arranged in a 2 × 2 factorial design, with 2 levels of Social procedure (Intermittent Social vs Continuous Social) and 2 levels of sipper Liquid (Ethanol vs Water).

For rats in the Intermittent Social groups, the sipper was inserted into the chamber for 10 s immediately before the presentation of the social stimulus, which consisted of the lifting of the guillotine door separating the experimental rat from the conspecific male rat in the wire mesh cage for 15 s. The wire mesh of the cage restricted physical contact between the experimental rat and the social stimulus rat. Rats in the Continuous Social groups received similar procedures, except that the guillotine door was open during the entire duration of the session, allowing the experimental rat continuous exposure to the conspecific male rat in the wire mesh cage during the entire session. For the Ethanol groups the concentration of ethanol in the sipper increased across sessions, while the Water groups received 0% ethanol (tap water) in the sipper throughout the experiment (see Table 1). Sessions were conducted with each ethanol concentration until session-to-session variability in mean g/kg ethanol intake for each of the ethanol groups did not vary by more than 10% between two

Table 1
Experimental procedures

| Sessions | Number of Sessions | Groups | | | |
|---|---|---|---|---|---|
| | | Intermittent Social/ Ethanol | Continuous Social/ Ethanol | Intermittent Social/Water | Continuous Social/ Water |
| 1–10 | 10 | 3% ethanol | 3% ethanol | Water | Water |
| 11–20 | 10 | 4% ethanol | 4% ethanol | Water | Water |
| 21–26 | 6 | 6% ethanol | 6% ethanol | Water | Water |
| 27–32 | 6 | 8% ethanol | 8% ethanol | Water | Water |
| 33–37 | 5 | 10% ethanol | 10% ethanol | Water | Water |
| 38–41 | 4 | 12% ethanol | 12% ethanol | Water | Water |
| 42–45 | 4 | 14% ethanol | 14% ethanol | Water | Water |
| 46–49 | 4 | 16% ethanol | 16% ethanol | Water | Water |

consecutive sessions. Upon completion of the daily session, rats were immediately removed from the chamber and returned to their home cage. Rats in the Intermittent Social groups [Intermittent Social/Ethanol ($n=10$) and Intermittent Social/Water ($n=10$) groups] received 35 trials per session. Each trial consisted of the insertion of the sipper for 10 s. The retraction of the sipper was accompanied by the lifting of the guillotine door, providing exposure to the social stimulus for 15 s. The mean inter-trial interval (ITI) was 60 s (±15 s), the mean interval between successive insertions of the sipper was 75 s, and the session duration was approximately 50 min. For rats in the Continuous Social groups [Continuous Social/Ethanol ($n=12$) and Continuous Social/Water ($n=8$) groups] the sipper was inserted for 10 s periods on the same schedule as for the Intermittent Social groups, but the guillotine door remained in the raised position, allowing the experimental rat continuous exposure to the social stimulus during the entire duration of the session. For all groups, the mean interval between successive insertions of the sipper was 75 s and the session duration was approximately 50 min. For both groups, volume of liquid consumed (ml) was determined by recording the liquid level in the tube to the nearest 0.5 ml immediately before and after each session.

### 2.5. Blood ethanol and plasma corticosterone assays

Immediately after the last (49th) session, all rats were sacrificed by rapid decapitation and trunk blood samples were taken. Samples were collected in heparinized tubes, centrifuged, frozen, and then assayed for blood ethanol levels by using ethyl alcohol test kit (Product #229-29, Diagnostic Chemicals, Ltd., Oxford, CT, USA). Duplicate samples were assayed for plasma corticosterone by radioimmunoassay (Corticosterone RIA kit, MP Biomedicals, Irvine CA, USA) using a tritium label for corticosterone and a highly specific corticosterone anti-serum, with a detection threshold of 0.1 μg/100 ml.

### 2.6. Statistical analysis

For subjects in each session, liquid consumed (ml) and body weight (kg) were recorded, and grams of liquid consumed per kilogram body weight (g/kg liquid intake) were derived. For the Ethanol groups, grams of ethanol consumed per kilogram body weight (g/kg ethanol intake) were also derived. Water groups received 0% ethanol (tap water) in the sipper on all sessions. For purposes of comparing fluid intake across the Ethanol and Water groups, all evaluations of liquid intake as a function of sessions are based on those sessions during which the Ethanol groups received the indicated concentrations of ethanol. Effects of sessions on initiation of liquid intake were evaluated by analyzing mean ml drinking and mean g/kg liquid intake on the last session (day 10) that the Ethanol groups received 3% ethanol in the sipper. Mean ml drinking and mean g/kg liquid intake during the last 4 sessions during which the sipper for the Ethanol groups contained each of the 8 concentrations of ethanol were derived. Effects on ml drinking, g/kg liquid intake, and body weight of Social procedure (Intermittent vs Continuous) and sipper Liquid (Ethanol vs Water) and Blocks of 2 ethanol concentrations (3%–4%, 6%–8%, 10%–12%, 14%–16%) were assessed by 3-way mixed-design $2\times2\times4$ repeated-measures univariate analysis of variance (ANOVA, Systat Statistical Software, Richmond, CA, USA). The mean of each block of 2 ethanol concentrations was based on the mean of the last 4 sessions with each ethanol concentration of that block. If the overall ANOVA revealed a significant 3-way interaction, further evaluations were conducted. For each factor, a separate 2-way mixed-design $2\times4$ repeated-measures univariate analysis of variance was conducted (ANOVA, Systat Statistical Software, Richmond, CA, USA). Fisher's Least Significant Difference (LSD) test provided pair-wise comparison at individual points (alpha = 0.05). Effects of Social procedure on mean blood ethanol levels (mg/dl) and mean plasma corticosterone levels were assessed by independent-measures Student's *t*-test (Systat Statistical Software, Richmond, CA, USA).

## 3. Results

### 3.1. Initiation of drinking from the sipper

All 40 experimental rats initiated drinking from the sipper during the first 10 sessions; however, there were no significant group differences in ml drinking or g/kg liquid intake during sessions 1–10. Analysis revealed no significant effects on mean ml drinking or on mean g/kg liquid intake of Social procedure or sipper Liquid on day 10 (all $P$'s $>0.05$).

### 3.2. Ethanol intake (g/kg)

Overall analysis of effects on g/kg liquid intake of Social procedure, sipper Liquid, and Blocks of ethanol concentrations revealed no significant main effect of Social procedure [$F(1,36)=1.158$, $P>0.25$], a significant main effect of sipper Liquid [$F(1,36)=27.861$, $P<0.01$], a significant main effect of Blocks of ethanol concentrations [$F(3,108)=35.699$, $P<0.01$], and a significant 3-way interaction between Social procedure, sipper Liquid, and Blocks of ethanol concentrations [$F(3,108)=4.084$, $P<0.01$]. Separate analyses were conducted to evaluate further this 3-way interaction.

The Intermittent Social procedure induced more g/kg ethanol intake than the Continuous Social procedure when the sipper contained the two highest Blocks of ethanol concentrations (10%–12% and 14%–16%). Analysis of effects on g/kg ethanol intake of Social procedure and Blocks of ethanol concentrations (see Fig. 1, top panel) revealed no significant main effect of Social procedure [$F(1,20)=3.949$, $P>0.05$], a significant main effect of Blocks of ethanol concentrations [$F(3,60)=118.446$, $P<0.01$], and a significant interaction effect between Social procedure and Blocks of ethanol concentrations [$F(3,60)=6.145$, $P<0.01$]. Fisher's LSD revealed that g/kg ethanol intake for the Intermittent Social/Ethanol group was significantly higher ($P<0.05$) than for the Continuous Social/Ethanol group at the two highest Blocks of ethanol concentrations (10%–12% and 14%–16%).

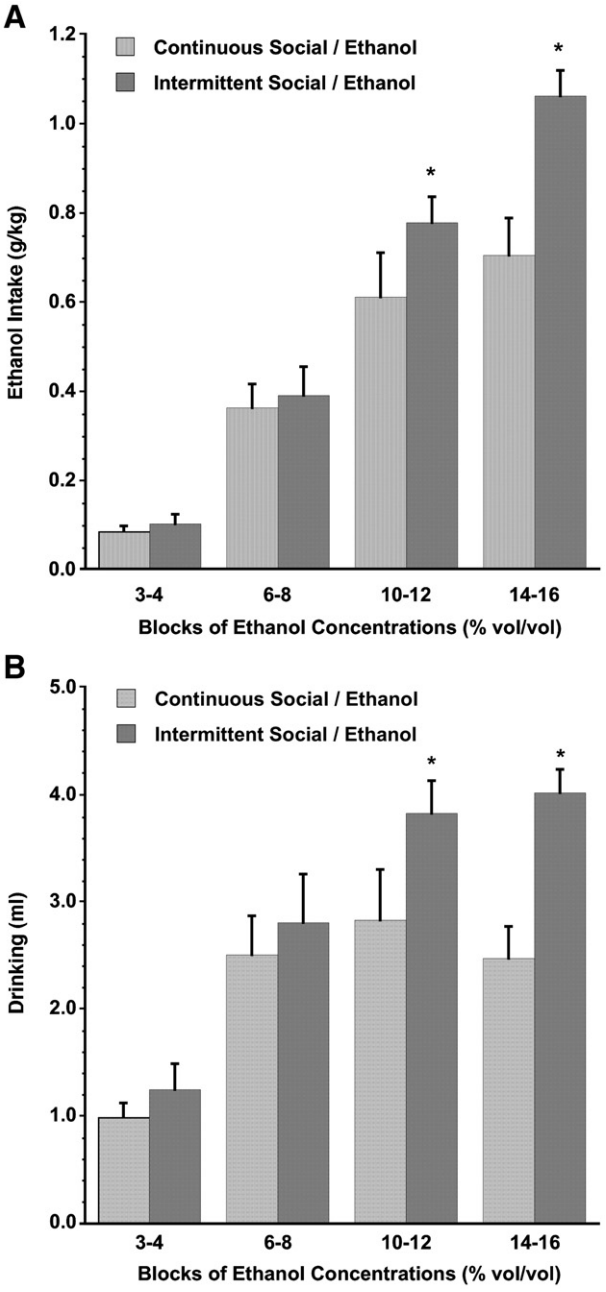



Fig. 1. Top panel: Mean daily grams of ethanol intake per kilogram body weight (g/kg) per daily session as a function of four Blocks of two ethanol concentrations each [3%–4%, 6%–8%, 10%–12%, 14%–16% (vol/vol)] for the Intermittent Social/Ethanol ($n=10$) and Continuous Social/Ethanol ($n=12$) groups. Means for each of the four Blocks of two ethanol concentrations [3%–4%, 6%–8%, 10%–12%, 14%–16% (vol/vol)] were derived from the last four sessions with each of the two concentrations of ethanol. The vertical bars represent the standard error of the mean. The asterisk (*) indicates the groups differed significantly (Fisher's LSD, $P<0.05$) during sessions with the 2 highest Blocks of ethanol concentrations [10–12% and 14–16% (vol/vol)]. Bottom panel: Mean milliliters (ml) of drinking from the sipper per daily session as a function of four Blocks of two ethanol concentrations each [3%/4%, 6%/8%, 10%/12%, 14%/16% (vol/vol)] for the Intermittent Social/Ethanol ($n=10$) and Continuous Social/Ethanol ($n=12$) groups. Means for each of the four Blocks of two ethanol concentrations [3%–4%, 6%–8%, 10%–12%, 14%–16% (vol/vol)] were derived from the last four sessions with each of the two concentrations of ethanol. The vertical bars represent the standard error of the mean. The asterisk (*) indicates the groups differed significantly (Fisher's LSD, $P<0.05$).

### 3.3. Ethanol liquid drinking (ml)

This effect of Social procedure was also observed in the ml drinking measure. The Intermittent Social procedure induced more ml drinking of the ethanol liquid than the Continuous Social procedure when the sipper contained the two highest Blocks of ethanol concentrations (10%–12% and 14%–16%). Analysis of effects on ml drinking of Social procedure and Blocks of ethanol concentrations (see Fig. 1, bottom panel) revealed no significant main effect of Social procedure [$F(1,20)=4.089$, $P>0.05$], a significant main effect of Blocks of ethanol concentrations [$F(3,60)=41.134$, $P<0.01$], and a significant interaction effect between Social procedure and Blocks of ethanol concentrations [$F(3,60)=3.720$, $P<0.02$]. Fisher's LSD revealed that the Intermittent Social/Ethanol group drank significantly more ml of the ethanol liquid than the Continuous Social/Ethanol group ($P<0.05$) at the two highest Blocks of ethanol concentrations (10%–12% and 14%–16%).

### 3.4. Water intake (g/kg)

The Intermittent Social/Water and Continuous Social/Water groups did not differ significantly in mean g/kg water intake on any of the Blocks of sessions during which the Ethanol groups received ascending concentrations of ethanol (see Fig. 2, top panel). Analysis of effects on g/kg water intake of Social procedure and the 4 Blocks of sessions during which the Ethanol groups received two ethanol concentrations each [3%–4%, 6%–8%, 10%–12%, 14%–16% (vol/vol)], revealed no significant main effect of Social procedure [$F(1,16)<1$], a significant main effect of Blocks of sessions [$F(3,48)=14.445$, $P<0.01$], and a significant interaction effect between Social procedure and Blocks of sessions [$F(3,48)=4.396$, $P<0.01$]. Fisher's LSD (alpha=0.05) revealed that the groups did not differ significantly during any of the 4 Blocks of sessions.

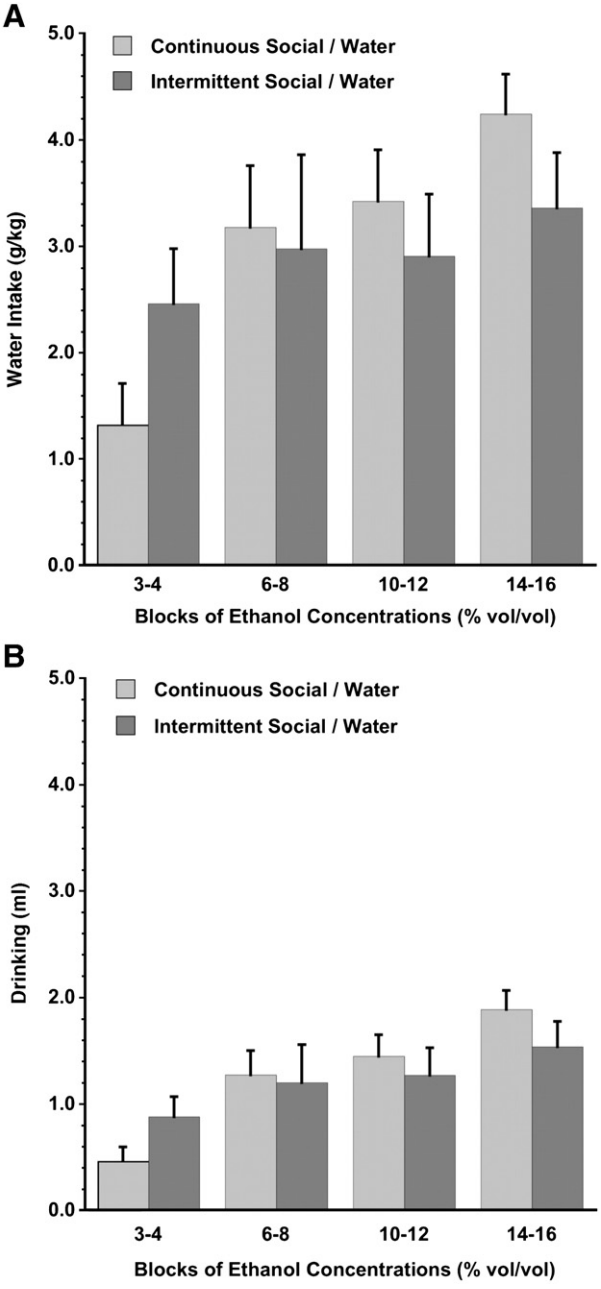
### 3.5. Water drinking (ml)

Analysis of the effects of Social procedure on ml water drinking yielded a similar pattern of results. The Intermittent Social/Water and Continuous Social/Water groups did not differ significantly in mean ml water drinking on any of the 4 Blocks of sessions during which the Ethanol groups received ascending concentrations of ethanol (see Fig. 2, bottom panel). Analysis revealed no significant main effect of Social procedure [$F(1,16)<1$], a significant main effect of Blocks of ethanol concentrations [$F(3,48)=24.822$, $P<0.01$], and a significant interaction effect between Social procedure and Blocks of ethanol concentrations [$F(3,48)=3.582$, $P<0.03$]. Fisher's LSD (alpha=0.05) revealed that the groups did not differ significantly during any of the 4 Blocks of sessions.

### 3.6. Liquid intake (g/kg)

In both the Intermittent and Continuous Social procedures, mean g/kg liquid intakes for the Ethanol groups were significantly higher than for the Water groups. Mean g/kg

liquid intakes (data not shown) for the Intermittent Social/Ethanol group were 3.5±0.5, 6.9±0.9, 8.8±0.8, and 8.9±0.6, for the 4 Blocks of ethanol concentrations (3%–4%, 6%–8%, 10%–12%, and 14%–16%), respectively. These liquid intake levels were consistently higher than those of the Intermittent Social/Water group (see Fig. 2, top panel). Analysis revealed a significant main effect of sipper Liquid [$F(1,18)=22.270$, $P<0.01$], a significant main effect of Blocks of sessions [$F(3,54)=21.913$, $P<0.01$], and a significant interaction effect between sipper Liquid and Blocks of sessions [$F(3,54)=13.196$, $P<0.01$]. Fisher's LSD revealed that g/kg liquid intakes for the Intermittent Social/Ethanol group were significantly higher ($P<0.05$) than for the Intermittent Social/Water group when the sipper contained the 3 highest Blocks of ethanol concentrations (6%–8%, 10%–12%, and 14%–16%).




Liquid intake was also higher in the Continuous Social/Ethanol group than in the Continuous Social/Water group. Mean g/kg liquid intakes (data not shown) for the Continuous Social/Ethanol group were 2.8±0.5, 6.5±0.9, 6.9±0.8, and 5.9±0.5, for the 4 Blocks of ethanol concentrations (3%–4%, 6%–8%, 10%–12%, and 14%–16%), respectively. These liquid intake levels were consistently higher than those of the Continuous Social/Water group (see Fig. 2, top panel). Analysis revealed a significant main effect of sipper Liquid [$F(1,18)=7.750$, $P<0.02$], a significant main effect of Blocks of sessions [$F(3,54)=15.669$, $P<0.01$], and no significant interaction effect between sipper Liquid and Blocks of sessions [$F(3,54)=2.064$, $P>0.10$].

### 3.7. Liquid drinking (ml)

In the Intermittent Social procedure analysis of effects on ml of liquid drinking revealed a significant main effect of sipper Liquid [$F(1,18)=23.722$, $P<0.01$], a significant main effect of Blocks of sessions [$F(3,54)=39.611$, $P<0.01$], and a significant interaction effect between sipper Liquid and Blocks of sessions [$F(3,54)=17.698$, $P<0.01$]. Fisher's LSD revealed that the Intermittent Social/Ethanol group drank significantly more ($P<0.05$) ml of liquid than the Intermittent Social/Water group at the three highest Blocks of Ethanol Concentrations (6%–8%, 10%–12%, and 14%–16%). In the Continuous Social procedure analysis of effects on ml of liquid drinking revealed a sigificant main effect of sipper Liquid [$F(1,18)=6.547$, $P<0.03$], a significant main effect of Blocks of sessions [$F(3,54)=20.245$, $P<0.01$], and no significant interaction effect between sipper Liquid and Blocks of sessions [$F(3,54)=2.073$, $P>0.10$].

### 3.8. Body weight

Overall analysis of effects on group mean body weight of Social procedure, sipper Liquid, and Blocks of sessions revealed no significant main effect of Social procedure [$F(1,36)=3.372$, $P>0.05$], no significant main effect of sipper Liquid [$F(1,36)<1$], a significant main effect of Blocks

Fig. 2. Top panel: The Intermittent Social/Water ($n=10$) and Continuous Social/Water ($n=8$) groups received water (0% ethanol) in the sipper throughout the experiment. Mean daily grams of water intake per kilogram body weight (g/kg) per daily session were derived from the last four sessions during which the Ethanol groups received each of the four Blocks of two ethanol concentrations each [3%–4%, 6%–8%, 10%–12%, 14%–16% (vol/vol)]. The vertical bars represent the standard error of the mean. There were no significant group differences in g/kg water intake at any of the Blocks during which the Ethanol groups received the indicated ethanol concentrations (Fisher's LSD, all $P$'s $>0.05$). Bottom panel: The Intermittent Social/Water ($n=10$) and Continuous Social/Water ($n=8$) groups received water (0% ethanol) in the sipper throughout the experiment. Mean milliliters (ml) of drinking from the sipper per daily session were derived from the last four sessions during which the Ethanol groups received each of the four Blocks of two ethanol concentrations each [3%–4%, 6%–8%, 10%–12%, 14%–16% (vol/vol)]. The vertical bars represent the standard error of the mean. There were no significant group differences in ml water drinking at any of the Blocks during which the Ethanol groups received the indicated ethanol concentrations (Fisher's LSD, all $P$'s $>0.05$).

of sessions [$F(3,108)=1049.616$, $P<0.01$], and no significant 3-way interaction between Social procedure, sipper Liquid, and Blocks of sessions [$F(3,108)=1.369$, $P>0.20$]. During the last 4 days during which the sipper for the Ethanol groups contained 3% ethanol (vol/vol), mean body weights for the 4 groups were in a range of 316 g to 328 g. During the last 4 days during which the sipper for the Ethanol groups contained 16% ethanol (vol/vol), mean body weights for the 4 groups were in a range of 428 g to 458 g.

### 3.9. Blood ethanol and plasma corticosterone levels

Mean blood ethanol levels were 107.6±18.8 mg/dl and 59.9±13.5 mg/dl for the Intermittent Social/Ethanol ($n=9$) and the Continuous Social/Ethanol ($n=12$) groups, respectively, and this difference was significant [$t(19)=2.12$, $P<0.05$]. Mean ethanol intakes were 1.05±0.01 and 0.81±0.12 g/kg on the day of sacrifice (day 49) for the Intermittent Social/Ethanol and Continuous Social/Ethanol groups, respectively. Mean plasma corticosterone levels were 187.0±44.2, 246.1±21.4, 208.2±49.0, and 264.8±28.9 ng/ml for the Intermittent Social/Ethanol, Continuous Social/Ethanol, Intermittent Social/Water, and Continuous Social/Water groups, respectively. Analysis revealed no significant main effects or interaction effects based on Social procedure or sipper Liquid (all $P$'s $>0.05$).

## 4. Discussion

The results indicate that when the sipper contained the two highest Blocks of ethanol concentrations (10%–12% and 14%–16%), the Intermittent Social procedure induced more ml ethanol drinking and more g/kg ethanol intake than the Continuous Social procedure. The data also show that this effect was particular to ethanol, as groups receiving Intermittent as compared to Continuous Social procedures did not differ in water drinking or g/kg water intake. Finally, the results indicate that during both Social procedures, there was more ml drinking and g/kg intake of the ethanol liquid than the water liquid.

The negative relationship, documented in the present study, between duration of exposure to a social stimulus and ethanol drinking, adds important information regarding the relationship between these factors. A positive relationship between social stimulation and ethanol drinking was reported in studies comparing ethanol drinking in groups receiving either intermittent presentations of a social stimulus or controls receiving no social stimulus (Tomie et al., 2004a, 2005). While the present study did not include a group receiving no social stimulus, the pattern of results across experiments indicates that the factor inducing rats to drink ethanol is the intermittent availability of the social stimulus, rather than the absolute amount of exposure to social stimulation.

It is appropriate to consider alternative interpretations of the finding that the Intermittent Social procedure induces more ethanol drinking than the Continuous Social procedure. One possible factor is differential spillage from the sipper during the session, but mean blood ethanol levels in samples obtained immediately post-session were significantly higher for the Intermittent Social group than for the Continuous Sipper group. Furthermore, if the results were due to spillage then water drinking should be higher in the Intermittent Social group compared to the Continuous Social group, and this was not observed. These data support the conclusion that differences in the volume of the ethanol liquid removed from the sipper during the session were likely due to group differences in ethanol drinking rather than spillage.

Another alternative interpretation is that elevated ethanol drinking in the Intermittent Sipper group is induced by the positive correlation between the sipper and the social stimulus. Less conducive to the induction of ethanol drinking is the zero correlation between the sipper and the social stimulus experienced by the Continuous Sipper group. The effects on ethanol drinking of the correlation between the sipper and the social stimulus have been evaluated in several studies wherein controls received presentations of the sipper and the social stimulus randomly with respect to one another (i.e., zero correlation procedures). Groups receiving the positive correlation procedures of the Intermittent Sipper group of the present study did not differ in any measures of ethanol drinking from controls receiving the sipper and social stimulus randomly (Tomie et al., 2004a, 2004b). This suggests that, in the present study, group differences in ethanol drinking are unlikely due to differences in the correlation between the sipper and the social stimulus.

Elevated ethanol drinking in the Intermittent Social group relative to the Continuous Social group resembles the effects of intermittent schedules of food presentations in studies of schedule-induced polydipsia (SIP) of ethanol drinking (Falk et al., 1972). In studies of SIP, intermittent food presentations induce more ethanol drinking than in non-intermittent controls that receive access to food pellets in a single massed ration (Reynolds et al., 1977; Tang et al., 1982). In several respects, the present data provide an atypical instance of SIP of ethanol drinking. All studies reporting SIP of ethanol drinking have employed intermittent presentations of food to induce ethanol drinking. The present data provide the first report of the induction of SIP of ethanol drinking that does not employ food as the inducing schedule. SIP of ethanol drinking maintained by intermittent presentations of food has been attributed to post-pellet prandial drinking (Cunningham and Niehus, 1997; Meisch and Thompson, 1974; Neill et al., 1994); however, prandial drinking does not provide an account of the elevated ethanol intake in the Intermittent Social group that was observed in the present study. All studies reporting SIP of ethanol drinking, have maintained rats on a strict regimen of food deprivation, typically to 80–85% of their free feeding weights, but in the present study, rats were maintained with free access to food and water in their home cages. Therefore, the present study reports, for the first time, SIP of ethanol drinking in non-deprived rats. This is an important observation, as SIP of ethanol drinking in hungry rats has been attributed to the caloric value of ethanol (Lester and Freed, 1973).

Both of the Social procedures induced rats to drink more of the ethanol solution than the water solution. This effect of the liquid in the sipper on liquid intake during Intermittent Social

procedures has previously been reported (Tomie et al., 2004a, 2005), and the present data extend this effect to situations wherein the social stimulus is presented continuously. The fluid effect is largely due to elevated levels of ethanol drinking; therefore, it is appropriate to comment on the elevated absolute levels of ethanol drinking, and particularly at the higher concentrations of ethanol, that were observed in the present study. It should be acknowledged that the elevated drinking of the higher concentrations of ethanol could be due to the use of an ascending series of ethanol concentrations, which allowed for acclimation to the effects of ethanol. On the other hand, an ascending series provides access to higher ethanol concentrations only when body weights are also higher, and this would tend to restrain measures of g/kg liquid intake in the ethanol groups.

The Long–Evans hooded rats employed in the present study are an outbred strain. When provided with an ascending series of ethanol concentrations, outbred strains of rats show steep declines in g/kg ethanol intake at concentrations above 10% (Bice et al., 1992; Holman and Myers, 1968; Kiefer and Dopp, 1989; Lucas and McMillen, 2002). Most notably, in the present experiment, Long–Evans hooded rats, an outbred strain, exhibited robust ethanol intake even as the concentration of ethanol in the sipper was increased from 10% to 16%. Several factors may have contributed to the high levels of drinking of higher concentrations of ethanol. One possible factor is the use of intermittent presentations of the ethanol sipper, a procedure that has been shown to induce more ethanol drinking than when the ethanol sipper is continuously available during the entire duration of the drinking session (Tomie et al., 2005, 2006). Another possible factor is the presence of a social stimulus during the ethanol drinking session, which has been reported to stimulate ethanol drinking (Tomie et al., 2004b, 2005). An additional feature of the present study that may have contributed to elevated ethanol drinking may be that the rats were housed in isolation in the colony room, receiving social stimulation only in the drinking chambers during daily drinking sessions. It is under conditions of social isolation in the colony room that the positively reinforcing effects of exposure to a social stimulus have been documented in rats (Evans et al., 1994). The social deprivation provided by the conditions of housing, in combination with the social stimulation provided only in the drinking chambers, may have induced more robust drinking of higher concentrations of ethanol than is typically observed in outbred strains of rats.

Unlike in previous reports (Hudson and Singer, 1979), these Social procedures had no systematic effects on water drinking. For the Intermittent Social/Water and the Continuous Social/Water groups, across the 4 Blocks, mean g/kg water intakes did not differ, indicating that intermittent presentations of the social stimulus did not induce SIP of water drinking. This is in contrast to the observations of Hudson and Singer (1979), who reported SIP of water drinking in monkeys using intermittent schedules of social stimulation. Their procedures differ in many ways from those of the present study, and these differences may have contributed to the discrepant findings. For example, the present study employed rats rather than monkeys, and, in the present study, the water sipper was presented on an intermittent schedule, whereas, in the experiments by Hudson and Singer (1979), the water sipper was continuously present during the entire duration of the session. In addition, in the present study the social stimulus was a proximal conspecific, free to move about within the adjacent wire mesh cage, while in the studies by Hudson and Singer (1979) the social stimulus was either a visual display of an image of a primate (Exp 1) or a monkey seated in a nearby chair (Exp 2).

The Intermittent Social procedure induced more ethanol intake than the Continuous Social procedure, but this effect was not observed with water. Several factors may have contributed to this finding. The absence of the social stimulus during the inter-trial interval of the Intermittent Social procedure may be aversive, stimulating ethanol drinking, but not water drinking. Another possibility is that the social stimulus may be arousing, and there may be more habituation to the social stimulus in the Continuous Social procedure, and this may reduce the tendency of the social stimulus to induce ethanol drinking, but not water drinking. While it is possible that the aversive properties of the absence of the social stimulus or habituation to the arousing-inducing properties of social stimulus have a selective effect only on ethanol drinking, there is no evidence from the data on plasma corticosterone levels of either aversive reactions or habituation effects.

Plasma corticosterone levels have been employed to index arousal (Merali et al., 1998; Tomie et al., 2002), and group differences in arousal due to social procedure or sipper liquid may result in differential drinking. In the present study, however, group differences in plasma corticosterone levels were not observed in post-session samples obtained immediately following the last daily session, indicating that if there were effects of arousal on drinking, they were not mediated by the release of corticosterone. On the other hand, corticosterone levels were not assessed repeatedly, and no measures were taken during the time that differences in drinking were emerging; therefore, it is possible that group differences in corticosterone levels were more likely to be observed at earlier times during the experiment.

Another possible mediator of the relationship between intermittent presentations of a social stimulus and their effects on ethanol and water drinking may be the form or duration of the interactions between the experimental subject and the social stimulus. In future studies, video recording of the topographies of the social interaction responses will provide data on the relationship between intermittent socializing and drinking of ethanol and water in these procedures.

## Acknowledgments

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

## References

Abrams DB, Niaura RS. Social learning theory. In: Blane HT, Leonard KE, editors. Psychological theories of drinking and alcoholism. New York: Guilford Press; 1987 . p. 131–78.

Bice PJ, Kiefer SW, Elder NB. Evaluating the palatability of alcohol for rats with measures of taste reactivity, consumption, and lick rat. Alcohol 1992;9: 381–7.

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

Cunningham CL, Niehus JS. Flavor preference conditioning by oral self-administration of ethanol. Psychopharmacologia (Berlin, West) 1997;34: 293–302.

Evans MJ, Duvel A, Funk ML, Lehman B, Sparrow J, Watson NT, Neuringer A. Social reinforcement of operant behavior in rats: a methodological note. J Exp Anal Behav 1994;62: 149–56.

Falk JL, Samson HH, Winger G. Behavioral maintenance of high concentrations of blood ethanol and physical dependence in rat. Science 1972;177: 811–3.

Holman BR, Myers RD. Ethanol consumption under conditions of psychogenic polydipsia. Physiol Behav 1968;3: 369–71.

Hudson R, Singer G. Polydipsia in the monkey generated by visual display schedules. Physiol Behav 1979;22: 379–81.

Institute of Laboratory Animal Resources. Guide for the care and use of laboratory animals, 1996;125pp. National Research Council, National Academy Press, Washington, DC.

Kiefer SW, Dopp JM. Taste reactivity to alcohol in rats. Behav Neurosci 1989;103: 1318–26.

Lester D, Freed EX. Criteria for an animal model of alcoholism. Pharmacol Biochem Behav 1973;1: 103–7.

Lucas L, McMillen BA. Conditioned taste aversion and the Myer's high-ethanol-preferring rat. Alcohol Alcohol 2002;37: 427–31.

Maisto SA, Carey KB, Bradizza CM. Social learning theory. In: Blane HT, Leonard KE, editors. Psychological theories of drinking and alcoholism. 2nd ed. New York: Guilford Press; 1999 . p. 106–57.

Meisch RA, Thompson T. Ethanol intake as a function of concentration during food deprivation and satiation. Pharmacol Biochem Behav 1974;2: 589–96.

Merali Z, McIntosh J, Kent P, Michaud D, Anisman H. Aversive and appetitive events evoke the release of corticotropin releasing hormone and bombesin-like peptides at the central nucleus of the amygdale. J Neurosci 1998;18(12): 4758–66.

Neill JC, Domeney AM, Costall B. Initiation and maintenance of oral ethanol self-administration in female Sprague Dawley rats. Alcohol 1994;11: 207–18.

Reynolds TJ, Kenny JT, Wright JW. A developmental study of schedule-induced polydipsia in the rat. Learn Motiv 1977;8: 284–8.

Tang M, Brown C, Falk JL. Complete reversal of chronic ethanol polydipsia by schedule withdrawal. Pharmacol Biochem Behav 1982;16: 155–8.

Tomie A, Silberman Y, Williams K, Pohorecky LA. Pavlovian autoshaping procedures increase plasma corticosterone levels in rats. Pharmacol Biochem Behav 2002;72: 507–13.

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.

Tomie A, Miller WC, Dranoff E, Pohorecky LA. Intermittent presentations of ethanol sipper tube induce ethanol drinking in rats. Alcohol Alcohol 2006;41: 225–30.