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Laboratory alcohol self-administration experiments do not increase subsequent real-life drinking in young adult social drinkers

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Abstract

Background—While the utility of experimental free-access alcohol self-administration paradigms is well-established, little data exist addressing the question of whether study participation influences subsequent natural alcohol consumption. We here present drinking reports of young adults before and after participation in intravenous alcohol self-administration studies.

Methods—*Timeline Follow-back* (*TLFB*) drinking reports for the 6 weeks immediately preceding the first, and the 6 weeks after the last experimental alcohol challenge were examined from subjects completing one of two similar alcohol self-administration paradigms. In study 1, eighteen social drinkers (9 females, mean age 24.1 years) participated in 3 alcohol self-infusion sessions up to a maximum *blood alcohol concentration* (*BAC*) of 160 mg%. Study 2 involved 60 participants (30 females, mean age 18.3 years) of the Dresden Longitudinal Study on Alcohol Use in Young Adults (*D-LAYA*), who participated in 2 sessions of alcohol self-infusion up to a maximum *BAC* of 120 mg%, and a non-exposed age- matched control group of 42 (28 females, mean age 18.4 years) subjects.

Results—In study 1, participants reported (3.7%) fewer *heavy drinking days* as well as a decrease of 2.5 *drinks per drinking day* after study participation compared to pre-study levels (p<. 05 respectively).. In study 2, alcohol-exposed participants reported 7.1% and non- alcohol-exposed controls 6.5% fewer drinking days at post-study measurement (p<.001), while *percent heavy drinking days* and *drinks per drinking day* did not differ.

Conclusion—These data suggest that participation in intravenous alcohol self-administration experiments does not increase subsequent real-life drinking of young adults.

Keywords

Timeline Follow- Back (TLFB); Computer Assisted Infusion System (CAIS); ethics; Family History of alcoholism (FH); alcohol self-infusion

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Introduction

Over the past several years, new methods for studying human drinking behavior have been established. Laboratory alcohol administration and self-administration research with non-treatment-seeking alcoholics has contributed significantly to our knowledge about basic mechanisms of alcohol use disorders, alcohol withdrawal, relapse to drinking, and the actions of pharmacological agents used to treat alcohol dependence (Dolinsky & Babor, 1997; Sinha et al., 1999; Zimmermann et al., 2013). Such alcohol administration research raises ethical concerns. One issue often discussed in the literature is whether the societal benefits of such experimentation outweigh the potential risks for the individual participant (Koocher, 1991; Modell et al. 1993; Dolinsky & Babor, 1997, Enoch et al., 2009). While immediate risks related to alcohol consumption itself exist (Wood & Sher, 2000), the more important question is whether participation in experimental alcohol administration leads to increased subsequent real-life drinking.

There is a small literature describing alcohol consumption in non-treatment-seeking alcoholics who had participated in laboratory studies involving alcohol administration. Sinha et al. (1999) measured post- study drinking of non-treatment-seeking alcoholics in a study testing the effect of naltrexone on oral alcohol self-administration. Assessing subsequent drinking with the *Timeline Follow-back interview* (*TLFB*; Sobell & Sobell, 1992), they found a significant decrease in the total number of *drinking days* as well as a reduction in the number of *drinks per drinking day*. Drobes and Anton (2000) presented similar results reporting significant reductions in drinking quantity and frequency 6 weeks after an alcohol challenge compared with the pre-study period in non-treatment-seeking people with alcohol dependence. As noted by Pratt and Davidson (2005), it is possible that these results were influenced by the anti-relapse medications that were administered in the above mentioned studies. Therefore, Pratt and Davidson (2005) performed an alcohol self-administration study without pharmacologic intervention in both non-treatment-seeking alcohol-dependent subjects and social drinkers. They found that, compared to the pre-study measurements, participants with alcohol-dependence reported significantly fewer *drinking days*, fewer *drinks per drinking day* and more *percent days abstinent* during the 6-week post-study period. Although they reported no differences for *percent days abstinent* and *drinks per drinking day* for social drinkers, a small but significant increase (3.5%) in *percent heavy drinking days* was discovered, which was attributed to the time of year the study was conducted. Using all data, Pratt and Davidson (2005) concluded that alcohol- challenge study participation did not increase drinking for either non-treatment-seeking alcohol dependent or social drinking subjects.

Taken together, the available literature suggests that participating in alcohol challenge studies does not increase drinking levels, cause later uncontrolled drinking, or relapse (see also Modell et al., 1993; Dolinsky & Babor, 1997), although each protocol included a brief motivational intervention (5 up to 45 minutes) at the end of the last experiment to encourage participants to decrease subsequent drinking and to seek counselling. There is a substantial body of evidence that brief interventions produce a significant effect and even show similar impact to that of more extensive interventions in reducing alcohol consumption, especially if used in health care and treatment settings including problem drinkers (for a review see Bien

et al., 1993). It is therefore possible that the reported reduction in post-study drinking in the described studies is driven by those interventions.

The standard method for laboratory alcohol self-administration is the oral route. However, while more naturalistic, oral consumption results in some unavoidable limitations. One problem is the between subjects variation of the maximum observed *blood alcohol concentration* (*BAC*) and the time of its occurrence (Ramchandani et al., 2009), thereby limiting the maximum subject alcohol exposures for safety purposes (typically around 90 mg%). Self-administration by alcohol infusions (e.g. Zimmermann et al., 2009; Plawecki et al., 2013) determined via physiologically-based pharmacokinetic modeling (Ramchandani et al., 1999; O'Connor et al., 2000; Plawecki et al., 2008) provides a tighter control of the prescribed time course of arterial *BAC* in every given subject and therefore reduces experimental variability while maximizing the bandwidth of exposure available to the subject. Although intravenous alcohol administration methods are becoming more common, no data is available addressing the question of whether these methods and route of administration affects later drinking by the participants. It is possible that, compared to studies using oral administration methods, participation in an intravenous administration challenge could result in altered subsequent drinking behavior.

We therefore obtained reports of real-life drinking before and after participation in two intravenously-delivered laboratory alcohol self-administration experiments involving different samples of healthy social drinkers. Besides the route of administration, our protocol differs from the previously published studies in 3 ways: (i), the participants were considerably younger, most of them being only 18 years old, (ii) there was no intervention to reduce drinking post-study, and (iii) study 2 included a control group of subjects who did not participate in the laboratory alcohol self-administration session.

Materials and Methods

Participants and recruitment

Study 1—For study 1, participants were recruited via local newspaper advertisements and the internet. Inclusion criteria were as follows: healthy male and female volunteers aged 18 to 35 years with at least one previous experience of alcohol intoxication (with either grossly disordered behavior, vomiting, blackout, or hangover), regular social drinking (defined by consuming alcohol at least once every 2 weeks throughout the preceding 2 months), being able to abstain from tobacco smoking for 4 hours without developing nicotine withdrawal, agreeing to abstain from any illegal drugs beginning 3 weeks before the first experiment, and effective contraception in women. Respondents were excluded if they had any physical or mental disorder requiring current medical treatment or psychotherapy, current or prior alcohol or illegal substance dependence, positive urine drug screening, usage of any medication interacting with alcohol over the past two weeks, premenstrual dysphoric disorder, pregnancy or intention to become pregnant, breast feeding, alcohol consumption with 24 hours of testing, known alcohol intolerance, and a history of epileptic seizures, viral hepatitis or HIV infection, liver or pancreatic disorders or laboratory tests indicating such disorders.

Forty-four respondents fulfilled all criteria. Fifteen participants declined participation after a telephone interview including description of study procedures. One male did not attend the first experiment day without providing a reason. Ten participants were lost to follow up. 18 (9 females, mean age 24.1 years) valid data sets were included in the final analysis.

Study 2—Study 2 involved participants of, or respondents to, the *Dresden Longitudinal Study on Alcohol Use in Young Adults* (*D-LAYA*), which investigates how a positive biological *family history* of alcoholism (*FH*) affects early drinking trajectories. Participants were recruited by postal mail invitation, which was sent to all (3.580) 18- and 19-year-old adults living in Dresden whose addresses were obtained from the Dresden residents' registration office. 63 participants were included in the alcohol exposure group. All *FH positive* respondents and an identical number of sex and smoking- matched *FH negative* respondents were considered for the alcohol exposure experiments. Age-matched surplus *FH negative* respondents were considered for the control group. Except for the different age criterion, all inclusion and exclusion criteria were identical across studies 1 and 2.

In the alcohol-exposed group, two participants were lost to follow-up and one female was excluded due to pregnancy related abstinence during the follow-up period. The non-exposed control group initially included 44 participants, two of which were lost to follow-up. Finally, we had 60 (30 females, mean age 18.3 years) valid data sets in the self-infusion group and 42 (28 females, mean age 18.4 years) in the control group.

Lab staff refrained commenting upon the subjects' drinking habits and gave no instructions whatsoever regarding the time between *TLFB* interviews. Sample size and subject characteristics for study 1 and study 2 are presented in Table 1.

General methods applying to both studies

Phone prescreening and laboratory screening session—The respondents were pre-screened via telephone for inclusion and exclusion criteria and likelihood of *Family History* (*FH*) status. During the laboratory screening session, subjects provided written informed consent, and a medical and psychiatric history was taken to confirm inclusion and exclusion criteria. For any substance which participants reported having used more often than 5 times in their life, the *Munich Composite International Diagnostic Interview* (*M-CIDI*; Lachner et al., 1998) substance abuse section questions were used to rule out substance dependence. *FH* was assessed using the *Family History Assessment Module* (*FHAM*) of the *Semi-Structured Assessment for the Genetics of Alcoholism* (*SSAGA*; Mann et al., 1985; Rice et al., 1995). Participants were classified as *FH positive* if they had at least one first-degree alcohol-dependent relative fulfilling three or more *DSM-IV* (American Psychiatric Association, 2000) alcohol dependence criteria in their lifetime, participants were classified as *FH negative* if none of their first-or second-degree relatives had been alcohol-dependent. A urine sample was obtained to screen for cannabinoids, cocaine, amphetamines, opiates and benzodiazepines and for pregnancy in women. Further, the number of alcoholic drinks consumed on each of the preceding 45 days was measured by using a computerized *Timeline Follow-back* (*TLFB*) assessment.

General alcohol self-administration methods

Urine drug and pregnancy screening (as described above) was repeated on all study days prior to the alcohol self-infusion experiment. Participants were instructed on the objectives of the alcohol infusion, namely to produce their preferred level of pleasant alcohol effects as they would do on a weekend party, and to avoid unpleasant effects. *CAIS* was used to determine the infusion profile of alcohol (6% v/v in saline) required to produce identical *BAC* increments in each participant (Zimmermann et al., 2008). To accustom participants to the self-infusion procedure, the experiment began with a 10 minute priming phase, during which the participants were asked to press a button 4 times in order to request 4 *BAC* increments, each of them lasting 2.5 minutes and raising *BAC* by 7.5 mg%. For the next 15 min, no more alcohol could be requested and *BAC* decreased from 30 mg% at a linear rate of −1 mg%/min, resulting in a *BAC* of 15 mg% at 25 min for all participants. This priming period was then followed by a 2 hour free-access self-administration phase, during which participants could increase their *BAC* by simple button-press, or refrain from doing so, at their discretion. Within the free-access self-administration phase, *BAC* readings were obtained every 30 minutes. Participants were free to watch taped sitcoms from a selection we offered, and use the bathroom. Once the 2 hour free-access phase was complete, the i.v. line was removed and participants were offered a full meal. Participants were required to remain in the laboratory until their *BAC* fell below 45 mg% (Zimmermann et al., 2009).

BAC measurements were obtained from breath alcohol samples using an Alcotest 6810 med breathalyzer (Draeger Sicherheitstechnik, Lübeck, Germany) applying the factor 210 to convert breath alcohol (mg/l air) to whole blood alcohol concentration (mg%). These readings correlate closely with arterial *BAC*, even prior to saturation of the distribution volume with alcohol, and therefore give a reliable estimate of brain alcohol exposure (Lindberg et al., 2007; Gomez et al., 2012).

Laboratory procedures specific to study 1

Participants underwent three laboratory sessions separated by a mean of 16.3 (SD=11.1) days. The first two sessions were as described above, with a *BAC* safety limit of 160 mg% (= 0.16% or 1.6‰). On the third session, the priming phase was replaced by an equivalent length infusion with goal of raising each individual's *BAC* to 75% of the maximum achieved on the second experimental day. Once complete, a 1.5-hour free access self-infusion phase ensued. During this free-access phase, participants were instructed to try to maintain their *BAC* at the same level by pressing or not pressing the button, using their subjective perception of alcohol effects.

Laboratory procedures specific to study 2

Alcohol-exposed participants underwent two testing sessions separated by a minimum of 7 days (mean and SD, 15.9 ±11.8). The first two sessions were as described above, with a *BAC* safety limit of 120 mg% (= 0.12% or 1.2). After the first two experimental days were complete,, a sub-sample of 30 young adults were selected to participate in two fMRI-imaging sessions investigating acute alcohol effects (60 mg% constant exposure or "clamp" vs. placebo) on behavioral control and brain perfusion (for details see Marxen et al., 2014; Gan et al. 2014).

Timeline Follow-back procedures

All participants underwent two *TLFB* assessments, where the number of alcoholic drinks consumed on each of the preceding 45 days was determined. The first *TLFB* assessment occurred during the laboratory screening session using a computerized self-report version of the *TLFB*. Subjects were instructed to enter the number of daily standard drinks containing 12 g of alcohol during the preceding 45 days into a Microsoft Excel form, making use of a conversion table and consulting their personal organizer. Alcohol-exposed participants of both studies were called forty-six days following their last experimental self-infusion day. After their first *TLFB* assessment, control group participants were informed about a later phone interview, but without revealing its purpose. A second TLFB assessment was performed during this phone interview, whereby control group participants were matched to alcohol-exposed participants in order to assess the same time period. All participants were reminded how to convert alcoholic beverages into standard drinks and to consult their personal organizer. Primary outcome measures of the *TLFB* were *percent drinking days*, mean *drinks per drinking day*, and *percent heavy drinking days*. *Percent heavy drinking days* was computed relative to the total 45 days of assessment and was defined by drinking 4 or more drinks per day in women and 5 or more drinks per day in men.

All procedures for both studies complied with the Declaration of Helsinki and were approved by the ethical committee of the Faculty of Medicine at the Technische Universität Dresden.

Statistical analysis

All analyses were conducted with *IBM SPSS Statistics 22* (IBM Corp., 2013) using standard procedures with their default settings. Demographic group characteristics were examined using *chi-square* and *t* tests. To compare real-life drinking before and after experimental alcohol exposure in study 1, we calculated a MANOVA to test the effect of the within-subjects factor time (pre-study vs. post-study) on the dependent *TLFB* variables *percent drinking days*, *drinks per drinking day*, and *percent heavy drinking days.* To compare real-life drinking between participants with and without experimental alcohol exposure in study 2, we included the between-subjects factor *group* (alcohol exposed vs. non-exposed) in the above described model. Finally, to explore the influence of potential confounding factors in both studies, we computed MANOVAs including the between-subjects factors *FH, sex, and smoking*. We calculated Pearson correlations to test for associations between the self-infusion measures (*mean and maximum achieved BAC, number of alcohol requests*) and the change in *TLFB* drinking outcomes.

Results

Study 1

Real-life drinking of participants with experimental alcohol exposure before and after study participation—Compared to their baseline *TLFB*, subjects reported less drinking after participating in the alcohol experiments as evidenced by a multivariate main effect of *time* in the MANOVA ($F(3, 15)=4.87$, $p<.05$). The corresponding univariate main effects of *time* revealed fewer *drinks per drinking day* ($F(1, 17)=9.60$, $p<.05$) and lower

percent heavy drinking days (F(1, 17)=4.52, p<.05) after study participation compared to pre-study levels (see Table 2).

Study 2

There were no *TLFB* differences between subjects who participated in the imaging sessions compared to those who did not (all p-values >.32). Consequently, results of all participants were analyzed in the same model.

Real-life drinking of participants with vs. without experimental alcohol exposure before and after study participation—Subjects reported fewer drinking days at the second *TLFB*- measurement compared to the first. MANOVA analysis demonstrated a main effect of *time* (F(3, 98)=13.08, p<.001) but no interaction of exposure *group* and *time*, indicating that differences between pre- and post-study drinking were not influenced by experimental alcohol exposure. The corresponding univariate main effect was obtained for *percent drinking days* (F(1, 100)=27.33, p<.001; see Table 2).

Additional Analyses of family history for alcoholism, sex, and smoking status —To identify potential confounds upon our results, *FH*, *sex*, and *smoking* status were analyzed though inclusion in the MANOVA models for each study. There were no significant interactions between *FH* and *time* nor *sex* and *time* upon drinking behavior in either study. While *smoking* did not influence the change in drinking behavior over time in study 1, the relationship in study 2 was more complex. MANOVA analysis including the factor *smoking* in study 2 identified a significant multivariate interaction of *smoking* × *group* × *time* (F(3, 96)=2.95, p<.05), with a corresponding univariate interaction affecting *drinks per drinking day* (F(1, 98)= 4.54, p<.05). Post hoc paired t-tests indicated that within the alcohol-exposed group, *drinks per drinking day* increased significantly for nonsmokers (t(23)=−2.44, p<.05), but decreased non-significantly in smokers. In the group that was not exposed to alcohol experiments, *drinks per drinking day* remained unaffected in nonsmokers and increased significantly in smokers (t(18)= −2.19, p<.05).

Correlation analyses between self-infusion variables and Timeline Follow-back drinking measures In both studies we found no correlations between any of the self-infusion measures (*mean and maximum achieved BAC, number of alcohol requests*) and the change in any *TLFB* drinking outcome (*percent drinking days, drinks per drinking day and percent heavy drinking days)* in participants with laboratory alcohol exposure.

Discussion

We presented two studies analyzing real-life drinking of young adults before and after participation in several alcohol self-infusion experiments.

In study 1, participants demonstrated significantly fewer *drinks per drinking day* and less *percent heavy drinking days* after laboratory alcohol exposure. In the larger study 2, participants reported significantly less *percent drinking days* in the second *TLFB* interview, independent of their laboratory alcohol exposure status.

Taken together, these results suggest that participation in laboratory studies with repeated intravenous alcohol self-administration does not increase subsequent alcohol consumption in 18- to 24-year-old young adult social drinkers. These results are consistent with several oral alcohol administration studies (e.g. Modell et al., 1993; Dolinsky & Babor, 1997; Drobes & Anton, 2000; Pratt & Davidson, 2005) which found no adverse effects on drinking or psychosocial functioning. Therefore, the use of intravenous self-infusion methods does not appear to promote drinking even in these rather young groups. This result is of considerable importance because increased alcohol consumption in late adolescence is associated with later alcohol problems including dependence (McCambridge et al., 2011), although it can normalize in young adulthood (e.g. Tucker et al., 2003).

When analyzing potential confounding variables, we found no influence of *FH* in laboratory alcohol exposed participants on post-study drinking behavior in both studies. Since *FH positive* subjects could be at increased risk of developing harmful drinking patterns (e.g. Edwards & Kendler, 2013), it is important to demonstrate that participation in alcohol challenge experiments does not additionally increase that risk. Further, we found no sex-related risk for increased drinking after experimental alcohol self-administration. Concerning the interaction between smoking status, time, and exposure group affecting drinks per drinking day in study 2, the post-hoc tests do not suggest a systematic pattern indicating which smoking group might be at increased risk. Most importantly, smokers who were exposed to alcohol did not increase subsequent drinking, although they might be at higher risk than nonsmokers.

Our study differed in several important ways from previous oral alcohol administration studies (Sinha et al., 1999, Drobes & Anton, 2000, Pratt & Davidson, 2005). First, our participants did not receive any intervention or counselling encouraging them to decrease their drinking. Because these brief interventions are known to be very effective (Bien et al., 1993), previous findings demonstrating less post-study drinking may be driven by these interventions. Consequently, our findings cannot be explained by the impact of such interventions. Second, our non-clinical sample in study 2 was drawn from a population registry, minimizing response bias. Therefore, our results should be generalizable to the population of non-dependent young male and female social drinkers without a psychiatric history. Third, study 2 included an age-matched control group without laboratory alcohol exposure. The fact that laboratory alcohol-exposed subjects did not report more drinking than those without such exposure demonstrates that unchanged post-experimental alcohol drinking cannot be attributed to repetition of the *TLFB*.

In both studies, we found no correlations between the pre- and post-study differences of the *TLFB* drinking measures and the alcohol self-infusion variables (*mean BAC*, *maximum BAC* and *number of drink requests*), indicating that single aspects of laboratory drinking behavior did not affect subsequent real-life drinking. Therefore, even young adults who tend towards risky alcohol consumption in the lab environment (reflected by high *BAC* values) are not at higher risk for increased real-life drinking due to alcohol study participation compared to average social drinkers.

The presented studies have several limitations. Study 1 had a relatively small sample size. Study 2 could only recruit *FH negative* subjects for the control group, therefore limiting the generalizability of the conclusions. Further, differences in *TLFB* administration may be a source of error. However, since the methodology was consistent across both groups of participants and prior research has demonstrated that the *TLFB* method can reliably assess daily drinking when administered by telephone or computer ($r > .77$; Hoeppner et al., 2010; Sobell et al., 1996), we believe the effect was minimal. As our observation period extended only over the first 45 days after the last alcohol experiment, we cannot exclude later subsequent increases in drinking. Additionally, because alcohol was intravenously administered, our conclusions are limited to drinking after infusion experiments. However, since subjective alcohol effects at a given *BAC* appear to be independent of route of administration (Ramchandani et al., 2004), it would follow that these results are generalizable to laboratory-based oral challenge experiments in young adults. Finally, there might have been unintended effects attributable to experimental setup: we instructed participants that they should consume alcohol to produce pleasant effects to their usual preferred level but some subjects may naturalistically drink for other purposes, such as to reduce negative affect. This instructional bias could have impacted experimental alcohol self-administration. Further, motivational differences in drinking behavior could relate to post-study alcohol consumption. Future study protocols should therefore provide more rigorous instructions to accommodate different drinking motives of participants. A related limitation is that all participants were explicitly told they will receive alcohol, which inevitably evokes alcohol expectancies that may markedly differ between subjects. To address these problems, future study designs should include the assessment of more subject characteristics associated with drinking motives (e.g. *Drinking Motives Questionnaire*; Cooper et al., 1999), alcohol expectancy (e.g. *Alcohol Expectancy Questionnaire*; Brown et al., 1987), or subjective response to identify possible subgroups which may have a higher risk of increasing their drinking behavior after participation in an alcohol self-infusion experiment.

In conclusion, the presented data suggest that laboratory alcohol self-infusion studies do not place young adults at risk for increased drinking and therefore can be safely used to advance laboratory alcohol research.

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Table 1

Sample characteristics of laboratory alcohol exposed participants and controls without experimental alcohol exposure.

	Study 1					
	Alcohol-exposed					
	Male (*N*=9)	Female (*N*=9)	Total (*N*=18)			
Mean (SD) Age	24.3 (3.2)	23.9 (3.9)	24.1 (3.5)			
%FH positive	55.6	55.6	55.6			
%Smokers	55.6	11.1*	33.3			
	Study 2					
	Alcohol-exposed			Non-exposed controls		
	Male (N=30)	Female (N=30)	Total (N=60)	Male (N=14)	Female (N=28)	Total (N=42)
Mean (SD) Age	18.2 (0.4)	18.3 (0.5)	18.3 (0.5)	18.4 (0.5)	18.5 (0.5)	18.4 (0.5)
%FH positive	26.7	43.3	35.0	0	0	0
%Smokers	60.0	60.0	60.0	57.1	39.3	45.2

*: significantly different from male participants at p<05.

FH positive=positive Family History of alcoholism; %*Smokers*=regular smokers.

Table 2

Study 1 and Study 2: Mean and SEM TLFB drinking variables covering the 45 days before (T1) and 45 days after (T2) alcohol self-administration experiments for laboratory alcohol exposed participants and the corresponding time period for controls without experimental alcohol exposure (study 2).

	Study 1 Alcohol-exposed (n=18)	
	T1	T2
PDD	24.3 ± 2.8	25.7 ± 1.8
D/DD	6.3 ± 0.9	3.8 ± 0.6*
PHDD	13.1 ± 1.9	9.4 ± 2.2*

	Study 1 Alcohol-exposed (n=60)		Non-exposed controls (n=42)	
	T1	T2	T1	T2
PDD	31.1 ± 2.3	24.0 ± 2.2***	27.7 ± 2.7	21.2 ± 2.3***
D/DD	4.1 ± 0.3	4.3 ± 0.3	3.5 ± 0.3	4.0 ± 0.4
PHDD	13.8 ± 1.6	13.3 ± 1.9	10.1 ± 2.0	10.3 ± 1.7

***: significantly different from T1 at p<001;

*: significantly different from T1 at p<05.

PDD=percent drinking days; *D/DD*=drinks per drinking day; *PHDD*=percent heavy drinking days (≥ 4 drinks per day for women, ≥ 5 drinks per day for men).